

Knee Kinematics and Kinetics During a Dynamic Balance Task and Gait in Those With and
Without Generalized Joint Hypermobility

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Symptomatic generalized joint hypermobility (GJH) is a life-long condition characterized by a predisposition to joint dislocations and subluxations, disturbed proprioception, chronic pain and fatigue, degenerative joint disease, and disability. Disease burden is amplified by delayed diagnosis which is, in part, due the current reliance on an invalidated diagnostic measure of symptomatic GJH, the Beighton Score. Biomechanics has the potential to improve the identification of GJH. While no patterns have emerged that appear specific to GJH in gait, stair climbing or vertical jumping, biomechanical characteristics of postural stability appear distinct in GJH.

The overall purpose of this study was to test whether performance of a dynamic balance test, the modified Star Excursion Balance Test (mSEBT), on stable and unstable surfaces, distinguishes between GJH and non-GJH in age and sex matched adults. A secondary objective was to determine the associations of performance on dynamic balance tasks with (i) the current diagnostic criteria and (ii) a measure of disease impact. It was hypothesized that maximum reach distance (MRD_{comp}) and maximum knee flexion angle (MKA_{comp}) would be smaller, and centre of pressure total excursion ($COPTE_{comp}$), dynamic knee stiffness (DKS) would be greater in those with GJH versus those without GJH. It was also hypothesized that disease impact would share a stronger association with MRD_{comp} than the current diagnostic criteria.

This cross-sectional study design compared two age (24.6 ± 4.1 years) and sex (26 females, 2 males) matched, non-athlete groups with and without GJH. From the entire sample, one participant met the criteria for symptomatic GJH. Kinematic and kinetic data were captured synchronously with research-grade motion capture (Optotrak Certus, Northern Digital Inc., Waterloo, ON, CA) and an in-ground force plate (OR6-7, Advanced Mechanical Technologies Inc., Watertown, MA, USA). First, participants performed a dynamic balance task, the mSEBT, in three conditions: stable (no foam surface), unstable (foam surface) and stable and timed. Performance on the mSEBT was measured. MKA_{comp} and $COPTE_{comp}$ were also measured during the mSEBT. Second, DKS was averaged over five gait trials at a

standardized speed (1.0 m/s). A two-way mixed analysis of variance was used to model the main effects of group and condition on for MRD_{comp} and MKA_{comp} and $COPTE_{comp}$. A Mann-Whitney U test was used to compare DKS in the non-dominant leg of both groups. Two hierarchical multiple regressions were used to determine if there is an association between (i) the current diagnostic criteria and MRD_{comp} , (ii) disease impact and MRD_{comp} , with physical activity (International Physical Activity Questionnaire) as a covariate.

No significant main effect was found between MRD_{comp} and group ($p = 0.26$), showing there was no difference between GJH and non-GJH groups in MRD_{comp} . No significant main effect was found between $COPTE_{comp}$ and group ($p = 0.99$), showing there was no difference between GJH and non-GJH groups in $COPTE_{comp}$. No significant main effect was found in MKA_{comp} between groups ($p = 0.45$), showing there was no difference between the amount of maximum knee flexion between non-GJH and GJH groups during the mSEBT. No significant difference was found between GJH and non-GJH groups for DKS in the timed condition ($p = 0.22$). The regression models identified that the diagnostic criteria (Beighton Score) ($R^2 = 0.07$; $p = 0.90$) and disease impact (Bristol Impact of Hypermobility Questionnaire) ($R^2 = 0.08$; $p = 0.95$) were not associated with MRD_{comp} .

The results of this study indicate performance on the mSEBT and DKS are not different in GJH than non-GJH groups in this sample of non-athlete university graduate and undergraduate students. Additionally, a measure of disease impact does not better associate with performance on the mSEBT than the current diagnostic criteria in this study's sample. Strengths of study include using a combination of novel clinical and biomechanical methods and measures in those with GJH. Future work on the clinical use of the mSEBT and DKS may consider recruiting those with symptomatic GJH and/or older participants with GJH.

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List of Abbreviations

5PQ	Five-Part Questionnaire for Identifying Hypermobility
BOS	Base of Support
BloH	Bristol Impact of Hypermobility Questionnaire
BMI	Body Mass Index
BS	Beighton Score
COMP	Composite Score
COP	Centre of Pressure
COPTE	Centre of Pressure Total Excursion
DKS	Dynamic Knee Joint Stiffness
EDS	Ehlers-Danlos Syndrome
G-HSD	Generalized Hypermobility Spectrum disorders
GJH	Generalized Joint Hypermobility
hEDS	Hypermobile Ehlers-Danlos Syndrome
HSD	Hypermobility Spectrum Disorders
IPAQ	International Physical Activity Questionnaire
JCOAP	Johnston County Osteoarthritis Project
JH	Joint Hypermobility
MKA	Maximum Knee Flexion Angle
MRD	Maximum Reach Distance
mSEBT	Modified Star Excursion Balance Test
OA	Osteoarthritis
NPRS	Numeric Pain Rating Scale
PFPS	Patellofemoral Pain Syndrome
POTS	Postural Orthostatic Tachycardia Syndrome
ROM	Range of Motion
SEBT	Star Excursion Balance Test

1 Introduction

Research and treatment of joint hypermobility-related disorders are complicated by diverse symptoms, unknown disease predictors, comorbidities and lack of clear etiology. In the most studied of these disorders, Ehlers-Danlos Syndrome (EDS) and Generalized Hypermobility Spectrum Disorders (G-HSD), common symptoms include chronic pain, chronic fatigue and recurrent joint dislocations and/or subluxations. The clinical sign of generalized joint hypermobility (GJH) is a common feature.

Heterogeneity in the number and location of affected joints as well as the degree and manifestation of pathological impacts make GJH difficult to identify and contributes to diagnostic delay (Castori et al., 2017; Malek et al., 2021). Difficulties in diagnosing GJH can be partially attributed to the current standard measure, the Beighton Score (BS). The BS is a clinician-scored, observational assessment of the presence or absence of GJH. It evaluates 4 bilateral joints plus the spine in one direction, in a mix of active and passive range of motion (ROM), with one point given for each hypermobile joint for a total score out of 9 (Appendix B). A BS indicating the presence of GJH is ≥ 6 for pre-pubertal children and adolescents, ≥ 5 for post-pubertal adults under 50 years of age and ≥ 4 for adults over 50 years of age (Castori et al., 2017; Juul-Kristensen et al., 2017; Malfait et al., 2017). Further, the BS has been invalidated as a method to indicate the presence or absence of GJH (Malek et al., 2021). Improving the diagnostic testing of GJH requires identifying characteristics of the population and having an accurate, clinically relevant, way to measure it.

Since the number, direction and location of joint hypermobility varies between individuals, identifying diagnostic approaches that focus on common impacts of GJH, such as recurrent subluxations, chronic pain and disability, may be helpful but is currently lacking. Partially, this is due to the lack of patterns in biomechanics of GJH in gait, stair climbing and vertical jumps. Only one study has attempted to characterize joints (e.g., soft tissue laxity/stiffness) in GJH populations, finding a qualitative difference between some tendons in GJH and non-GJH samples (Alsiri et al., 2019). Common findings for GJH are reduced proprioception and altered postural control as well as significant levels of pain and fatigue

(Kalisch et al., 2020; Smith et al., 2013). The current study measured kinematics and kinetics in a clinically relevant and accessible test of dynamic balance in those with and without GJH. It also compared the outcome of the dynamic balance test to diagnostic criteria (BS) and a validated measure of disease outcome. The goal of this was study to was to help inform the development of a more valid clinical measure of GJH and help characterize joints of those with GJH.

2 The Clinical Signs and Symptoms of Generalized Joint Hypermobility and its Associated Disorders

2.1 Definitions

Generalized Joint Hypermobility (GJH). Joint hypermobility (JH) is the capacity of a joint to actively and/or passively move beyond normally expected ROM) (Levangie et al., 2019). *GJH is the simultaneous presence of JH in multiple (usually five or more) major and minor joints in the axial skeleton and all four limbs* (Castori et al., 2017; Malek et al., 2021). While these terms are not diagnoses, JH and GJH are descriptors of clinical signs. JH and GJH can be isolated findings or indicators of an underlying syndrome and can be asymptomatic or symptomatic (Castori et al., 2017; Malek et al., 2021). There is some evidence showing that joint hypermobility can be acquired through intense, prolonged flexibility training in dancers (Klemp & Chalton, 1989). However, there has been no research comparing acquired and hereditary GJH. Unless it can be shown to be caused by injury, surgery, pregnancy, or intensive training, GJH is considered hereditary (Castori et al., 2017).

While most people with GJH are asymptomatic, others may experience periodic problems related to hypermobility or develop persistent symptoms (Grahame, 1999). Factors influencing symptom onset in individuals with asymptomatic GJH are currently unknown. Determining if GJH is asymptomatic or symptomatic is complicated by low levels of awareness of the clinical presentation of GJH in healthcare settings, methods of assessing JH, lack of prospective research, unknown pathogenesis, and heterogeneity of clinical presentation (Castori et al., 2017; Kalisch et al., 2020).

Symptomatic GJH. Symptomatic JH and GJH are categorized as either Hypermobility Spectrum Disorders (HSD), when symptoms are generally limited to the musculoskeletal system, or Hypermobile Ehlers-Danlos Syndrome (hEDS), when symptoms are multisystemic (Castori et al., 2017). While GJH is common in all 13 types of EDS, hEDS is the only type without an identified gene. A diagnosis of hEDS involves genetic testing to exclude other types of EDS and connective tissue diseases and relies on clinical evaluation of signs and symptoms (Castori et al., 2017; Malfait et al., 2017). The four types of

HSDs are intended to capture the spectrum of symptomatic JH in terms of severity and/or pattern of musculoskeletal involvement (Table 1). Peripheral HSD (P-HSD) is limited to the hands and feet. Localized HSD (L-HSD) is limited to a single body part or joint. Historical HSD (H-HSD) is identified by assessing history of hypermobility and excluding other rheumatological diagnoses. Finally, Generalized HSD (G-HSD) is symptomatic generalized joint hypermobility that does not meet the criteria for hEDS (Castori et al., 2017).

Symptom profiles, epidemiology, severity and impact of peripheral, localized and historical HSD has not been fully explored since their introduction in 2017. Methods of separating peripheral and localized JH/HSDs from the effect of injuries, accidents, physical activity, and other underlying conditions have yet to be determined. H-HSD is a category for those with acquired joint limitations (e.g., amputation, surgery) and cannot be assessed for GJH by traditional methods like the BS, which evaluates JH in four bilateral joints and the spine (Malfait et al., 2017). In these cases, the Five-Part Questionnaire for Identifying Hypermobility (5PQ), which has been validated against the BS, is used for diagnosis (Hakim & Grahame, 2003; Malfait et al., 2017). There is no difference between G-HSD and hEDS in terms of severity of musculoskeletal symptoms, physical functioning, impact on quality of life impact and treatment (Aubry-Rozier et al., 2021; Coussens et al., 2022; Tinkle et al., 2017).

Separating types of symptomatic GJH from asymptomatic GJH is difficult due to the indistinguishable clinical presentation of G-HSD and hEDS, delays in diagnosing GJH-related symptoms and unknown factors that may contribute to unmitigated disease worsening including joint soft tissue degeneration, chronic pain, chronic fatigue and/or disability. As a result, the focus this research was on individuals with GJH (both asymptomatic and symptomatic) but who have not been diagnosed with a hereditary connective tissue disorder other than hEDS.

Table 1. Types of hypermobility on the hypermobility spectrum as per the 2017 diagnostic criteria with expected Beighton Score outcome and musculoskeletal involvement. Adapted from Castori et al. (2017). All non-asymptomatic types of hypermobility are included in the term symptomatic GJH (S-GJH). * = Types of hypermobility included in this study.

Type of Hypermobility	Beighton Score	Musculoskeletal Involvement	Location of Hypermobile Joints
* Asymptomatic Generalized Joint Hypermobility (A-GJH)	Positive	Absent	Major and minor joints in the axial skeleton and all four limbs
Asymptomatic Peripheral Joint Hypermobility (A-PJH)	Usually negative	Absent	Hands and feet
Asymptomatic Localized Joint Hypermobility (A-LJH)	Negative	Absent	Single body part or joint
*Generalized Hypermobility Spectrum Disorder (G-HSD)	Positive	Present	Major and minor joints in the axial skeleton and all four limbs
Peripheral Hypermobility Spectrum Disorder (P-HSD)	Usually negative	Present	Hands and feet
Localized Hypermobility Spectrum Disorder (L-HSD)	Negative	Present	Single body part or joint
Historical Hypermobility Spectrum Disorder (H-HSD)	Negative	Present	Historical presence of JH, location of JH not indicated
*Hypermobile Ehlers-Danlos Syndrome (hEDS)	Positive	Possible	Major and minor joints in the axial skeleton and all four limbs, plus positive family history and/or systemic manifestations

2.2 Prevalence

Prevalence estimates are impacted by changes made to the diagnostic criteria for symptomatic GJH in 2017. Changes included adapting the criteria for GJH to account for the inverse relationship between age and BS scores, narrowing the diagnostic criteria for hEDS and introducing HSD (Castori et al., 2011; Malfait et al., 2017). Comparing prevalence before and after the 2017 criteria and between studies is complicated by a lack of uniformity of BS testing procedure and cut-off scores, sample sizes, and demographics (Juul-Kristensen et al., 2017; Malfait et al., 2017; Sobhani-Eraghi et al., 2020). Unless otherwise noted, prevalence rates are reported below according to BS cut-off scores from current diagnostic criteria.

Overall, prevalence for GJH has been reported worldwide at 3-36%, with the highest prevalence in children, decreasing with age and more prevalent in post-pubertal females (Kumar & Lenert, 2017; Russek & Errico, 2016; Saremi et al., 2020; Sobhani-Eraghi et al., 2020; Tinkle et al., 2017; Zhong et al., 2021). Prevalence rates of GJH have been reported as 17% for adults aged 15-39 years (Seow et al., 1999), and in two American university student populations at 12.5% (18-25 years) (Reuter & Fichthorn, 2019) and 26.5% (17-26 years) (Russek & Errico, 2016). There is some evidence supporting higher rates of GJH in non-Caucasians (Saremi et al., 2020; Singh et al., 2017).

Symptomatic GJH is less prevalent than asymptomatic GJH and depends on proper diagnosis, which is often delayed, sometimes to an age when hypermobility has diminished. One estimate suggests that 1 in 10 people with GJH develops symptoms (Hakim & Sahota, 2006), while another states that 3.3% of females and 0.6% of males with GJH are symptomatic (Kumar & Lenert, 2017). In a population level study of primary care or hospital-coded diagnosis of hEDS/HSD in Wales prevalence was 1 in 500, and therefore not a rare disease (Demmler et al., 2019). In a study, which did not depend on primary care diagnosis, prevalence was 19.5% for symptomatic GJH compared to 26.5% for asymptomatic GJH in 17-26 year old American university students (Russek & Errico, 2016). The proportion of symptomatic GJH is higher in patients with chronic fatigue syndrome and/or fibromyalgia than in healthy populations (Alsiri et al., 2023; Nijs, 2005; Nijs et al., 2006). High proportions of patients with symptomatic GJH have been reported in pain (39%) and rheumatology (37%) clinics, which may indicate a misclassification of multiple joint pain as GJH-related in the pre-2017 diagnostic criteria and/or the need for multi-modal care for those with symptomatic hEDS/HSD (To et al., 2017). Joint pain, re-injury and prolonged rehabilitation time contributes to a higher proportion (55%) and more frequent visits to physiotherapy clinics for patients with GJH compared to those without GJH (Clark & Simmonds, 2011).

2.3 Diagnosis

The purpose of identifying GJH is initiating treatment and management of articular symptoms and diagnosing symptomatic JH. Taking a medical history and physical examination has three goals:

screening for GJH, assessing the burden of symptoms and excluding other GJH-related connective tissue diseases (Kumar & Lenert, 2017). Yet, tests of joint ROM and self-reported questionnaires are used to evaluate JH. There is no gold standard for evaluating GJH (Malek et al., 2021). The most widely cited tools for evaluating GJH are the BS and the Five-Part Questionnaire for Identifying Hypermobility (5PQ). The BS is the most common test for GJH used in research studies and clinical settings. It is also used to indicate the presence or absence of GJH in diagnostic criteria for EDS and HSD (Table 1) (Castori et al., 2017; Malek et al., 2021; Malfait et al., 2017; Simmonds, 2022).

2.3.1 Identifying Generalized Joint Hypermobility

The BS is a clinician-scored, observational assessment of the presence or absence of GJH. It evaluates 4 bilateral joints plus the spine in one direction, in a mix of active and passive ROM, with one point given for each hypermobile joint for a total possible score of 9 (Appendix B). Prior to 2017, the BS cut-off score for all ages was ≥ 4 ; this cut-off represented an arbitrary score without evidence (Malek et al., 2021). In 2017, diagnostic criteria were updated reflecting the relationship between BS and age so that a positive BS for GJH is ≥ 6 for pre-pubertal children and adolescents, ≥ 5 for post-pubertal adults under 50 years of age and ≥ 4 for adults over 50 years of age, reflecting the inverse relationship between age and BS (Castori et al., 2017; Juul-Kristensen et al., 2017; Malfait et al., 2017).

The reference cited for these cut-off scores is a systematic review of GJH assessment methods by Juul-Kristensen and colleagues (2017) who found a wide variety of BS testing protocols and scoring in clinical and research assessments and made recommendations with the intent of fostering uniformity. Recommendations were based on the most widely used cut-off scores in the highest quality studies and the relationship between BS and age (Juul-Kristensen et al., 2017). While accepting the age-based BS scoring and citing Juul-Kristensen and colleague's (2017) work on BS testing, the 2017 diagnostic criteria description of the BS does not include the recommendation that cut-off scores for adults should include historical presence of BS-assessed JH (Juul-Kristensen et al., 2017; Malfait et al., 2017). The most recent clinical recommendations suggest using the BS and 5PQ when assessing GJH (Morlino & Castori, 2023).

Morlino & Castori (2023) include the 5PQ to screen for historical HSD and JH, but it is unclear whether the authors suggest that a patient history of hypermobile joints be considered for non-historical HSD. Very few research studies published before and after the 2017 diagnostic criteria ask study participants about the historical presence of GJH when using the BS. The exclusion of historical JH in assessing all types of GJH may weaken the ability of the BS to detect GJH in those with JH-related joint damage and hypomobility. It remains unclear if and, if so, how, GJH diagnosis should account for historical presence of JH in joints assessed by the BS, which contributes to the ongoing non-uniformity in clinical diagnosis and research studies of GJH.

2.3.2 Hypermobile Ehlers-Danlos Syndrome and G-HSD

Diagnosis of hEDS requires the simultaneous presence of three criteria: 1) GJH as assessed by the BS; 2) the exclusion of other connective tissue, rheumatological disorders or alternative diagnoses for hypermobility; and 3) a combination of two out of three categories of features including systemic manifestation of a generalized connective tissue disorder, family history of hEDS and musculoskeletal complications (Malfait et al., 2017). G-HSD is diagnosed as a positive BS, the presence of at least one musculoskeletal symptom but not satisfying the criteria for hEDS. Nevertheless, subsequent investigation may identify multi-systemic involvement, which would result in a shift in diagnosis from G-HSD to hEDS (Castori et al., 2011).

2.3.3 Beighton Score

Intended to be a screening tool for GJH, in practice, the BS is used to indicate the presence or absence of GJH. Originally, the BS was an epidemiological survey of musculoskeletal conditions and joint mobility conducted in 1973 in one African village (Beighton et al., 1973). The method of joint ROM evaluation was selected because it was simple, did not require equipment and made it easy to perform quantitative measures. The authors used it as a descriptive tool, concluding that those with hypermobility would score higher compared those without hypermobility (score of 0-3 out of a possible 9) and that there was relationship between joint pain and a higher score (Beighton et al., 1973). Adopted by the

researchers, clinicians and authors of JH diagnostic criteria, the BS is intended as a screener to be supplemented by a more thorough examination of suspected GJH. However, clinical knowledge of symptomatic hypermobility is lacking and the BS is used as an all-or-nothing indicator of GJH (Kalisch et al., 2020; Malek et al., 2021).

The strengths of the BS remain its ease of use in clinical settings and inter-rater reliability higher than other measures of GJH, but questions of its validity remain (Juul-Kristensen et al., 2017; Malek et al., 2021). A 2017 review of four test assessments (BS, Carter and Wilkinson (CW), Hospital del Mar (HdM), Rotes-Querol (RQ)) and two questionnaires (5PQ, Beighton Score self-reported (BS-self)) for classifying GJH concluded that the BS was the best available GJH assessment tool even though there was insufficient evidence showing its validity (Juul-Kristensen et al., 2017). The 2017 diagnostic criteria adopted several recommendations from this systematic review but excluded the recommendation that a positive score on the BS should be given if a person has a negative score on an item but answers yes when asked “Have you been able to do this previously?” (Castori et al., 2017; Juul-Kristensen et al., 2007, 2017; Malfait et al., 2017). (Juul-Kristensen et al., 2017; Malfait et al., 2017). A 2023 invited review includes previous presence of hypermobility only within the context of diagnosing historical HSD or JH. The authors recommend using both the BS and the 5PQ when screening for hypermobility. (Morlino & Castori, 2023). The 5PQ is validated against the BS but does not assess all 9 joints in the BS. Excluding historical JH in assessing all types of GJH may weaken the ability of the BS to detect GJH in those with JH-related joint damage and hypomobility. While JH may be historical, GJH symptoms may be lifelong. Very few research studies published before and after the 2017 diagnostic criteria ask study participants about the historical presence of GJH when using the BS. It remains unclear if GJH diagnosis should account for historical presence of JH in joints assessed by the BS, which contributes to the ongoing non-uniformity in clinical diagnosis and research studies of GJH.

Guidelines for measuring joint range of motion further highlight the inconsistencies in clinical usage of the BS. While measuring joint range of motion with goniometers “should” be used for BS when

possible, one of the benefits of the BS is that it does not require tools or very much training (Morlino & Castori, 2023). Type of goniometer, level of expertise, angle size being assessed are all factors that impact measurement error (Brosseau et al., 1997; Hancock et al., 2018; Lenssen et al., 2007; van Rijn et al., 2018). Validity has not been tested for the joint angles in the BS and most studies do not report the use of goniometers. In the knee and elbow, measurement error has been reported as equal to or greater than the BS cut off of 10° of extension (Brosseau et al., 1997; Hancock et al., 2018; Lenssen et al., 2007). On a clinical level, expertise and availability of goniometers vary by workplace and specialty (e.g., general practice GP, physiotherapy). Additionally, reliability and validity of goniometer use has been largely done with those trained in physiotherapy (Brosseau et al., 1997; Hancock et al., 2018; Lenssen et al., 2007), but physiotherapists cannot confer a diagnosis. Physicians diagnose HSD and hEDS using the BS. The difference between the diagnostic criteria, the reference used for the BS protocol, the most recent recommendations (BS and 5PQ) and its use in clinical settings leaves room for continued non-uniformity in BS testing. Heterogeneity in study methodology persists, preventing Malek and colleagues (2021) from performing a meta-analysis on the clinical usage of the BS.

While Juul-Kristensen et al. (2017) deemed the BS the most reliable assessment tool for GJH, reliability of the BS to detect the presence or absence of GJH in adults is in doubt (Malek et al., 2021). In a literature review, Malek et al. (2021) showed that the BS lacks validity, sensitivity, specificity and reliability in adult populations. Validity is the measured accuracy of test against a gold standard. There is no gold standard for assessing JH and validity of the BS has been shown only for children aged 6 to 12 (Smits-Engelsman et al., 2011). Its specificity (the ability to identify those with GJH) is lacking because the BS does not correlate equally with minor and major joints in all four limbs and the axial skeleton. It correlates poorly with JH in the lower limb and shoulder, and correlates well with the JH in the thumb and wrist. Sensitivity of the BS (the ability to identify those without GJH) is poor because the assessed joints, which are only assessed in one plane of movement, does not reflect the distribution, location and type of joints affected by GJH (Malek et al., 2021). The BS cannot discriminate between localized and

generalized hypermobility for those under 50 years and between localized, peripheral and generalized for those over 50 years (Malek et al., 2021).

Another key criticism of the BS is the value of the item assessing spine hypermobility (“palms on the floor”) but involving multiple joints in the forward flexion maneuver. In children, this item is excellent at identifying those with GJH (specificity = 93.66%), but is a very weak indicator of those without GJH (sensitivity = 13.84%) (Corten et al., 2020). Brock & Hamonet (2015) examined muscle, tendon and aponeurosis retraction in the hamstring muscles of 232 patients with hEDS aged 2 to 70. Using the Lasègue maneuver (patient is lying supine and the examiner lifts the patient’s straight leg until encountering resistance), retraction was defined as $\leq 80^\circ$ angle between an exam table and the patient’s outstretched leg. Results showed that 87.5% of those with hEDS had hamstring retraction that prevented 97.8% of them from performing the “palms on the floor” item from the BS tests but did not affect knee hyperextensibility (Brock & Hamonet, 2015), casting doubt on the usefulness of this item in GJH assessment.

2.3.4 Other tests of Generalized Joint Hypermobility

Other tests of GJH, such as the Upper Limb Hypermobility Assessment Tool and Lower Limb Assessment Score, assess a greater number of joints in multiple planes and more joints that are affected in GJH than the BS. These have been validated in adult populations but have yet to be tested as diagnostic tools (Meyer et al., 2017; Morlino & Castori, 2023; Nicholson & Chan, 2018; Schlager et al., 2018; Simmonds, 2022). These tests require more time, equipment and expertise to implement than the BS. Since the BS is required for GJH diagnosis, the use of these tests is recommended for cases in which clinical judgement is that a negative BS did not accurately exclude GJH (Simmonds, 2022). While it may seem ideal to recommend that the diagnostic criteria be revised to include one of these alternate assessments, ultimately, all these tests give a score based on the number of hypermobile joints. Malek and colleagues (2021) point out that, if the purpose of diagnosis is to identify the impact of the disease, than simply counting the number of hypermobile joints does not measure disease impact nor can it

identify GJH as a the cause for painful joints in those who have lost their hypermobility due to age, accident or injury (Malek et al., 2021; Malfait et al., 2017).

Two validated questionnaires offer alternatives to simply counting hypermobile joints. First, the 5PQ is a self-report tool validated against the BS and consists of five questions (Appendix C). A score of two or more on the 5PQ suggests symptomatic JH with 84% sensitivity and 80-89% specificity (Hakim & Grahame, 2003). The 5PQ is included in the hEDS diagnostic criteria for individuals who have acquired joint limitation (e.g., surgery, amputation, etc.) that impacts BS assessment and in diagnosis of historical HSD (Castori et al., 2017; Malfait et al., 2017; Morlino & Castori, 2023). Since there are no prospective studies tracing the progression of joint hypermobility over time, the 5PQ is not a validated measure on its own and is used for those who physically cannot perform the BS and those evaluated for historical HSD (Castori et al., 2017; Morlino & Castori, 2023). Since the 5PQ was validated against the BS, it reflects the strengths and deficiencies of the BS as described above. Second, the Bristol Impact of Hypermobility Questionnaire (BIOH) has known-group validity, in this case meaning the ability to discriminate between groups with and without symptomatic GJH (Palmer et al., 2020).

2.3.5 Delayed diagnosis

The possibility that symptomatic GJH is underdiagnosed (Palmer et al., 2020) is strengthened by the difficulties in diagnosing a group with heterogeneity in the number and location of affected joints, degree and manifestation of pathological impacts, a poor understanding of how symptom presentation changes over time and documented diagnostic delay (Castori et al., 2017; Demmler et al., 2019). Clinically, patients living with HSD/hEDS present with pain related to multiple joints and/or diffuse pain but, in the early stages, radiographs are normal, which may add to delays in diagnosis (Ericson & Wolman, 2017). A 17-year population level cohort study in Wales showed an average of 14 years between clinical manifestations of symptoms and diagnosis and a delay of more than 28 years for 25% of patients (Demmler et al., 2019).

2.3.6 Disease progression

Diagnostic delay impacts the disease progression and symptom management. Delayed diagnosis is a determinant of pain and fatigue and may contribute to maladaptive movement patterns (Kalisch et al., 2020; Krahe et al., 2018; Palmer et al., 2016). Compared to those childhood diagnosis, patients diagnosed in adulthood have a greater number of diagnosed comorbidities including circulatory and mental disorders and a higher odds for prescription drugs use (Demmler et al., 2019). When surveyed, most people with GJH are not satisfied with diagnosis and disease management and can have negative psychological impact due to trivialization of symptoms, misdiagnosis and improper treatment (Krahe et al., 2018; Palmer et al., 2016).

Only one study has investigated disease progression in symptomatic GJH and identified three phases based on common symptom presentations (Castori et al., 2011). The first phase, “hypermobility,” is characterized by congenital contortionism and clumsiness/motor delay. The second phase, “pain,” involves the onset of chronic fatigue, chronic and/or recurrent joint and muscle pain and tendonitis and the continuation of dislocations and recurrent sprains/strains. The third phase is “stiffness,” characterized by loss of joint hypermobility, worsening of pain and disability, the onset of sleep disturbances, tendon ruptures, various functional gastrointestinal issues, tachycardia and limb paresthesia (numbness or tingling) (Castori et al., 2011; Rombaut et al., 2015). Phases of disease progression are based on observational data which identifies, but does explain the associations of, clusters of symptoms common in symptomatic GJH. Since some elements of the diagnostic criteria are influenced by age (e.g., Beighton Score), reassessment of childhood diagnosis in adulthood and periodic monitoring may be necessary (Morlino & Castori, 2023). Presenting with distinct but overlapping multisystemic issues, like hEDS and postural orthostatic tachycardia syndrome (POTS) (an autonomic nervous system disorder), can often result in diagnostic delays or misdiagnosis (Do et al., 2021; Mathias et al., 2021).

3 Impact of Symptomatic Generalized Joint Hypermobility

3.1 Comorbidities

Symptomatic joint hypermobility is characterized by diverse extra-articular systemic manifestations (e.g., secondary musculoskeletal, nervous and cardiovascular systems, skin, mucosae, fascia), accumulating in number over time and may be expressed as an abnormal body structure (Castori et al., 2017). The impact of these comorbidities varies widely between individuals and the connection between these co-morbidities and JH is complicated by acquired factors such as physical activity, occupation, accidents and other factors. The most common non-articular co-morbidities associated with JH include psychological distress, POTS, pelvic and bladder dysfunction and functional gastrointestinal disorders (Castori et al., 2017).

3.2 Secondary Musculoskeletal Manifestations

Articular manifestations of JH are considered mechanical consequences of JH (Castori et al., 2017). The major categories of musculoskeletal complications and manifestations cited in the 2017 classification of joint hypermobility are the following: micro- and macro-trauma, degenerative joint and bone disease, disturbed proprioception, possible muscle weakness, and musculoskeletal physical traits. Macro-traumas are hypermobility-related isolated or recurrent trauma (e.g., dislocations, subluxations, soft tissue injuries) resulting in acute pain, loss of function and the need for immediate treatment. Micro-traumas are injuries from repetitive stress to tissues that usually go unnoticed until, over time, they may lead to acute persistent or chronic pain and possibly early joint degeneration (Castori et al., 2017). The silent nature of micro-traumas makes measuring injury rates in asymptomatic and symptomatic GJH challenging and, as a result, micro-traumas are not always accounted for in studies of injury and GJH (Russek & Errico, 2016).

A cluster of musculoskeletal traits common in those with GJH, like valgus deformity of the elbows and non-congenital scoliosis, may be a result of mechanical forces being applied to lax soft tissue (Castori et al., 2017). Besides one study using strain elastography and showing some qualitative

difference in the tendons of those with GJH compared with those without GJH (Alsiri et al., 2019) there have been no investigations into the tissue mechanics of hypermobility. In the absence of experimental data on the soft tissue of those with GJH, the source of the laxity (e.g., ligaments, tendons, cartilage and/or other collagen-rich rich structures) remains unknown.

Joint hypermobility and osteoarthritis. JH may be associated with osteoarthritis (OA). The differing results of studies investigating a link between osteoarthritis (OA) and JH can be partially by the choice of JH assessment. Four studies used data from the Johnston County Osteoarthritis Project (JCOAP), an ongoing, community-based, prospective cohort study of OA and OA risk in the United States. These studies found no association between OA and GJH. These studies assessed their participants, aged 45 and older with and without OA, using a BS cut-off score of 4 (Flowers et al., 2018; Golightly et al., 2019; Goode et al., 2019; Gullo et al., 2019). The historical presence of GJH was not assessed. Since GJH is not a primary focus of the JCOAP, considerations of factors that likely affected the ROM of people with GJH in their cohort (e.g., surgeries, injuries or joint degeneration, repetitive joint trauma) were likely outside the scope of the project. The use of historical data may also have limited their assessment of GJH. Since the JH assessment in the JCOAP-related studies may be incomplete the results should be read with caution.

Specific methodological choices were observed among studies that found a relationship between OA and GJH. These choices reflected a more homogeneous sample (additional exclusion criteria), tiers of BS cut-off scores or used the 5PQ. A study of 22-92-year-olds (BS ≥ 4) excluding major trauma and inflammatory rheumatological diseases found a higher frequency of people with knee OA and GJH than those using data from the JCOAP (Gürer et al., 2018). In a group of 101 people in their 60s diagnosed with hand OA, results showed a relationship between moderate hypermobility (BS ≥ 2) and hand OA and a trend linking moderate and severe isolated carpal-metacarpal 1 involvement and a BS ≥ 4 (Jónsson & Valtýsdóttir, 1995). In a study investigating first early detection of carpometacarpal OA, women aged 30-50 years were separated into high and low hypermobility scores based on the 5PQ. Magnetic resonance

imaging showed the group with high hypermobility had more abnormalities in trapezium and metacarpal cartilage and trapezium bone (Taylor-Gjevre et al., 2022).

3.3 Muscle Function

Muscle strength and proprioception influence muscle function in GJH and can contribute to activity limitation and disability in symptomatic GJH (Castori et al., 2017). The cause of muscle weakness in those with GJH has not yet been identified. There is conflicting evidence about muscle strength and GJH which may be impacted by the presence of pain. In groups with asymptomatic GJH and groups that have both symptomatic and asymptomatic GJH, no difference was found in maximum in voluntary contraction of knee extensions, knee flexor and extensor strength, or muscle power (Ewertowska et al., 2020; Jensen et al., 2013; Mebes et al., 2008; Radaelli et al., 2022). However, in groups of symptomatic GJH muscle strength and endurance were significantly lower than non-GJH groups (Coussens et al., 2022; Sahin, Baskent, Ugurlu, et al., 2008) with differences in lower extremity weakness as much as -30-49% (Rombaut et al., 2012). Robbins et al. (2020) found lower isometric strength in those with EDS (mostly hEDS) in hip flexors and abductors and ankle flexors and extensors but not in knee flexion or extension. No differences in muscle mass were found between symptomatic GJH and control groups, which may indicate that weakness and/or pain caused muscle dysfunction (Coussens et al., 2022; Rombaut et al., 2012).

Poor proprioception is common among those with symptomatic GJH but the mechanisms underlying the relationship are unknown (Castori et al., 2017). Proprioception is the sense of a joint in relation to other joints and in space. A 2013 meta-analysis identified five studies with 254 participants and revealed reduced proprioception in lower limbs, including reduced knee proprioception in young females (Smith et al., 2013). Two studies showed poorer threshold detection to movement (Rombaut, Paepe, et al., 2010; Sahin, Baskent, Cakmak, et al., 2008). Three studies showed poorer joint position sense in GJH compared to non-GJH groups (Smith et al., 2013). Comparing GJH groups with and without non-specific neck pain (BS \leq 4, aged 20-45), increased cervical joint position error (poorer proprioception)

was found in those with non-specific neck pain (Reddy et al., 2022). Study participants with higher BS scores had increased cervical joint position error and less neck muscle endurance than those with lower BS scores (Reddy et al., 2022). Scheper et al. (2016) found that proprioception confounded the relationship between muscle strength and activity limitations, implying that reducing activity limitations may improve both proprioception and muscle strength. Knee proprioception was similar in between groups of symptomatic GJH and those with chronic fatigue syndrome (Nijs et al., 2006), leaving open the question of confounding factors in GJH-related proprioceptive deficits.

3.5 Pain

Pain is common in symptomatic GJH. Pain in GJH is most often chronic and widespread but may be regional or widespread, recurrent or acute (Chopra et al., 2017; Engelbert et al., 2017). Pain may start as localized and be described as more acute (e.g., dislocations), usually appearing first in the lower limb. The rate of reported arthralgias in those with GJH increases from approximately 30% in children aged 0-10 to greater than 80% for those over 40 (Castori et al., 2013; Chopra et al., 2017). In a survey of 2,354 participants with symptomatic and asymptomatic JH (25-107 years, JH = 5PQ >2), those with JH were more likely to suffer from chronic widespread pain and, after adjusting for age and sex, were 40% more likely to report severe widespread pain than non-JH (Mulvey et al., 2013). Of those with hEDS, studies have reported high proportions experience joint pain (up to 100%), muscle pain (around 90%), limb pain (91%) as well as a large proportion with a simultaneous diagnosis of fibromyalgia (42%) (Kalisch et al., 2020). Neck pain and headaches are also common. Those with HSD/hEDS may be at higher risk for pelvic pain (Ali et al., 2020; Chopra et al., 2017; Kalisch et al., 2020).

Pain intensity is generally moderate or severe, higher in asymptomatic GJH than controls, highest in symptomatic GJH and contributes to below average physical functioning and psychological distress (Kalisch et al., 2020; Rombaut et al., 2015; Scheper et al., 2016). Generalized hyperalgesia (pain sensitization), pain coping mechanisms and vigilance may play a similar or even larger role in pain-related impacts of GJH on quality of life than pain intensity (Rombaut et al., 2015; Scheper et al., 2016).

Joint pain from injuries, trauma or joint degeneration is the most frequent and severe symptom of GJH. The cause of joint pain in JH is most frequently cited as a consequence of the predisposition to repetitive and/or occasional micro- and macro- musculoskeletal trauma. In the context of GJH, the association of pain and joint trauma is most clearly documented in temporomandibular joint dysfunction, but has not been shown in other joints (Castori et al., 2017; Malfait et al., 2017; Rombaut, Malfait, et al., 2010). Keer and Simmonds (2011) suggested that poor posture, maladaptive movement patterns, poor proprioception, the tendency for those with JH to rest at end range of motion in an effort to increase stability, and strains of the tissues supporting the joint may contribute to pain and fatigue (Keer & Simmonds, 2011). In a study of an outpatient clinic for hEDS (pre-2017 criteria), Kalisch et al. (2020) found that diagnostic delay, being “professionally active” and thoughts of helplessness increased the likelihood of severe pain. Pain also had a moderate association with disability in adults and adolescents with symptomatic GJH (Scheper et al., 2016).

While pain is the primary factor that separates asymptomatic and symptomatic GJH, the mechanism underlying GJH-related pain is currently unknown. However, the presence of musculoskeletal pain simultaneously with GJH does not indicate symptomatic GJH because there is no current clinical test to confirm a causal relationship (Morlino & Castori, 2023). Since chronic pain from any source and GJH have similar prevalence and joint hypermobility with pain occur in non-hypermobility related disorders, GJH-related pain needs to be identified by excluding other causes (Morlino & Castori, 2023).

3.6 Fatigue

Compared to control groups, fatigue is greater in asymptomatic GJH and greatest in symptomatic GJH (Scheper et al., 2016). Fatigue is present in approximately 86% of those with symptomatic GJH, 62.7-79.5% of whom reported severe fatigue (Kalisch et al., 2020; Krahe et al., 2018; To et al., 2019). Psychological, physical and physiological factors influence the presence and severity of fatigue. In those with symptomatic GJH, fatigue has stronger association with disability than pain. Fatigue also contributes to several factors that negatively affect quality of life including malaise, sleep disturbances, poor

concentration, lower self-efficacy and self-worth, anxiety and depression (Scheper et al., 2016; To et al., 2019).

Several factors associated with fatigue severity may impact physical activity. Krahe et al. (2018) identified five predictors of increased fatigue severity: higher self-reported level of joint pain, orthostatic dizziness related to heat and exercise, lower levels of physical activity, lower levels of participation in personal and community relationships and dissatisfaction with the process of diagnosis and symptom management options (Krahe et al., 2018). Voermans et al. (2011) identified a positive correlation between fatigue and muscle weakness but not with self-reported maximum walking distance. Differing results of the impact of fatigue on physical activity may be a result the different tools used to measure activity. An association was found when a self-reported index of physical activity (composite score = intensity X duration X frequency) was used (Krahe et al., 2018) while no association was found when self-reported maximum walking distance and a measure of physical activity impairment (Sickness Impact Profile) was used to measure activity (Voermans et al., 2011).

Two studies have investigated the mechanism of fatigue and its effect on biomechanical outcomes during muscle contraction and gait. One study investigated the contribution of central versus peripheral fatigue in symptomatic GJH. Applying electrical stimulation to the peripheral nerve of the biceps brachii and transcranial magnetic stimulation over the motor cortex in subjects 29-45 years old, To et al. (2019) found that during a fatiguing protocol the symptomatic GJH group ($BS \geq 4$) showed central but not peripheral fatigue and the control group ($BS \leq 4$) did not display either types of fatigue. Another study showed that fatigue was associated with gait abnormalities symptomatic GJH ($n = 11$) and control ($n = 20$); but, it may be possible that this study was underpowered and it lacked a description of the fatigue protocol (Celletti et al., 2012). Future work investigating loaded joints perhaps in a position or movement that challenges joint stability may shed further light on nature of fatigue in GJH.

3.7 Kinesiophobia

In GJH, fatigue, pain and kinesiophobia (i.e., fear of movement and/or reinjury) are closely related. Kinesiophobia is common in musculoskeletal disorders, occurring in 61-93% of adults diagnosed with symptomatic GJH, and is a feature of the “stiffness” phase of GJH (Celletti et al., 2013; Kalisch et al., 2020; Rombaut et al., 2015). Avoidance of activities may focus on movements that increase risk injury, subluxations and/or feelings of joint instability associated with pain (Keer & Simmonds, 2011). Kinesiophobia correlates with pain but is unrelated to pain severity in adults with hEDS (Celletti et al., 2013; Kalisch et al., 2020). Kinesiophobia has a strong relationship with fatigue severity, leading to a cycle of pain-kinesiophobia-fatigue where pain-induced avoidance and fear of movement leads to detraining that contributes to fatigue (Celletti et al., 2013; Simmonds et al., 2019).

3.8 Disability

Disability (a patient-reported outcome of restriction in daily functioning) is a significant concern for some with GJH. The impact of disability on asymptomatic GJH is mild while those with symptomatic GJH have severe and clinically relevant levels of disability (Scheper et al., 2016). Of a sample of 75 adults at an hEDS hospital clinic, 65% of patients self-reported a high level of mobility disability. Adults with hEDS or HSD score worse than the rest of the United States (US) population on many health-related quality of life item and symptom self-management (Estrella & Frazier, 2024). GJH is highly prevalence in pain, physiotherapy and rheumatology clinics (Clark & Simmonds, 2011; To et al., 2017). Common GJH co-morbidities (fibromyalgia, chronic fatigue syndrome, OA) also contribute physical ability and psychological well-being (Nijs, 2005; Nijs et al., 2006). Perceived disability in GJH is similar to populations with rheumatoid arthritis, OA, low back pain and other musculoskeletal disorders. In Canada and the United States, those with HSD and hEDS have low satisfaction with healthcare, which is associated with lower health-related quality of life and symptom management self-efficacy (Estrella & Frazier, 2024; Guedry et al., 2023). Disease burden is similar to fibromyalgia and greater than rheumatoid arthritis (Rombaut et al., 2011; Scheper et al., 2016).

Several factors contribute to disability in GJH. A 2016 meta-analysis on pain and symptomatic GJH in adults and adolescents found a moderate correlation between disability and pain ($r = 0.64$, $p = 0.02$) and strong correlations between disability and fatigue ($r = 0.912$, $p = 0.01$), and anxiety and depression ($r = 0.86$, $p = 0.02$) (Scheper et al., 2016). Symptomatic GJH often leads to maladaptive compensatory patterns, particularly in posture, that could exacerbate pain and diminish quality of life (Palmer et al., 2016). Activity limitation is affected by muscle strength and proprioception in symptomatic GJH (Bates et al., 2021b; Scheper et al., 2017) and those with GJH have diminished levels of regular physical activity, significantly lower sport participation and lower health-related quality of life than controls (Rombaut et al., 2011). Disability is worsened for those with central pain sensitization (generalized hyperalgesia) (Rombaut et al., 2015).

4 Factors that Contribute to the Presence and Severity of Symptomatic Generalized Joint Hypermobility

4.1 Genetics

EDS is a heritable connective tissue disorder with three broad characterizations: joint hypermobility, skin hyperextensibility, and tissue fragility. The subtypes of EDS are genetically and clinically heterogeneous and share features with other connective tissue disorders. Genetically, all types of EDS except hEDS are identified by mutations of collagen-encoding genes or genes encoding collagen-modified enzymes. Proteins associated with these genes are called “causative proteins” and the subtypes are grouped by the pathways in which these proteins function (Malfait et al., 2017). Although hEDS is the only one of the 13 types of EDS without an identified gene, the current hypothesis for pathogenesis is a genetically-induced collagen biosynthesis that results in a “disorganized extracellular matrix”(Malfait et al., 2017).

The current understanding of hEDS genetics is that of pleiotropy, meaning that a single gene or gene-gene interaction causes several seemingly unrelated phenotypic traits that make up the syndrome. GJH is considered a mechanical consequence of altered gene expression in hEDS. The most common extra-articular traits associated with hEDS are psychological distress, cardiovascular dysautonomia (often in the form of POTS), functional gastrointestinal disorders and pelvic and bladder dysfunction (when other causes have been excluded). Patterns of JH-related musculoskeletal manifestations are highly variable and can present clinically at different ages because they are mediated by, but not caused by, genetically induced JH (Castori et al., 2017). Castori et al. (2017) describes these as secondary effects modified by JH and can include sex, mechanical forces, accidents, occupation, and physical activity.

The theory of pleiotropy in hEDS is accepted but there is little evidence supporting a genetic connection to joint laxity. Beckley et al. (2022) found an association between knee hyperextension in the non-dominant legs of a healthy population and a gene-gene interaction of three collagen genes (*COL5A1*, *COL11A1* and *COL11A2*). Knee joint laxity was measured with passive and active knee extension in a

supine position with a goniometer, anterior-posterior tibial translation using an arthrometer and tibial internal-external rotation with a Robotic Knee Testing device. The authors note gene-gene interactions are different for those measured with knee hyperextension (Beckley et al., 2022). Narrowing the diagnostic criteria in 2017 was, in part, an effort to help isolate the gene(s) associated with hEDS.

4.2 Age

Prevalence of GJH is highest in children and decreases with age. There is an inverse relationship between BS and age (Castori et al., 2011; Seow et al., 1999; Singh et al., 2017; Tinkle et al., 2017). Some studies have shown a consistent rate of decrease in BS similar over the lifespan (Seow et al., 1999; Singh et al., 2017) while others show that BS falls more rapidly in childhood than adulthood (Beighton et al., 1973). In the only study on disease progression, Castori et al. (2011) noted a dramatic decrease in those with symptomatic GJH at the age of 33. The implication of Castori et al.'s (2011) work is that there may be an age (maybe around 33 years old) after which diagnosis of symptomatic GJH becomes more complicated and less likely.

The interaction of age at diagnosis and disease progression has not yet been investigated. Due to heterogeneity of symptoms and the unique nature of Castori et al.'s (2011) study on disease progression, clear age ranges are not known for each disease phase except for the first phase which occurs at 0-10 years of age. Based on age of symptom onset the second phase could occur from ages 11-30 and the third phase may begin after the age of 30 (Castori et al., 2011). Demmler et al. (2019) found a significant difference of 8.5 years between the age of diagnosis of males and females with more males diagnosed under the age of 18. Reasons for the differences in sex were beyond the scope of Demmler et al.'s (2019) study. Recent studies suggest that variability and coordination during gait is present in adults but not in children with symptomatic GJH (Robbins et al., 2022; Vermeulen et al., 2022); but it is unclear if these gait biomechanics represent disease progression. Further work is needed to identify the associations between age, sex and disease progression.

4.3 Sex

GJH is more common in post-pubertal females than males. There is no statistical difference in GJH prevalence between the sexes in until post-puberty or 14 years of age (Singh et al., 2017) after which the rate of decrease in joint mobility may be more pronounced in males (Castori et al., 2011). In a study of GJH in American university students there was no overall difference in prevalence between the sexes but there was a higher proportion of males with a BS of 0 and a higher proportion of females with non-zero BS (Reuter & Fichthorn, 2019). There may also be sex differences in distribution of affected joints (as assessed by the BS), particularly in the spine, right knee, and elbows (Reuter & Fichthorn, 2019).

Clinical presentation of symptomatic GJH is similar between the sexes (Castori et al., 2011), but there are relatively more females with symptomatic GJH. In a population study in Wales, Demmler et al. (2019) noted 70% of those diagnosed symptomatic GJH were female. Russek & Errico (2016) noted higher proportions of females in asymptomatic GJH (24.5% of females, 13.7% of males) and symptomatic GJH (36.7% in females and 13.7% in males) in a population of university students 17-26 years of age. Females are seen in higher proportion in rheumatology clinics for hypermobility-related symptoms (Castori et al., 2011; Grahame, 1999; Hakim & Grahame, 2003; Seow et al., 1999). Yet, fewer females (41%) are diagnosed during childhood than males (72%) (Demmler et al., 2019), which may lead to poorer disease management, more pain and greater overall physical and psychological disease burden on females (Kalisch et al., 2020; Palmer et al., 2020).

4.4 Ethnicity

GJH may be less prevalent in Caucasians than non-Caucasians (Juul-Kristensen et al., 2017; Malfait et al., 2017; Morlino & Castori, 2023; Singh et al., 2017; Zhong et al., 2021), though variability between studies make it unclear if ethnicity is a risk factor (Klemp et al., 2002; Reuter & Fichthorn, 2019; Seow et al., 1999). The reporting, and when reported, the categorization of ethnicity is inconsistent between studies. North American studies tend to define ethnicity as a Caucasian, Black, Asian, Hispanic and Other/More than one ethnicity (Reuter & Fichthorn, 2019; Russek & Errico, 2016) or

Caucasian/European and non-Caucasian (Singh et al., 2017), while studies in Asian and the Middle East describe ethnicities not identified in Western studies such as an Persian, Azeri, Kurdish and Lur in Iran (Saremi et al., 2020) or Malay, Indian and Chinese in Singapore (Seow et al., 1999). This could suggest that there is variability between geographic or national populations with different ethnic makeups or between studies. Direct comparisons of measures prevalence and/or impact of GJH between ethnicities are complicated by variations in BS cut-off, non-reporting of BS protocol and the absence of measured and/or reported ethnicity in many studies. It remains unclear if the difference between ethnic groups is presence/absence of GJH, impact of disease or results from non-uniform measures of GJH and/or ethnicity.

4.5 Pregnancy

Joint laxity and BS increase during pregnancy, peaking in the second trimester and continuing postpartum (Cherni et al., 2019; Chu et al., 2019; Opala-Berdzik et al., 2018). Joint laxity tends to reduce postpartum, but the length of pregnancy-related laxity has not been identified. Increased joint laxity relative to early pregnancy has been detected 4 and 6 months postpartum (Cherni et al., 2019; Chu et al., 2019). In a prospective study examining multiplanar knee laxity and compliance of women from the first trimester of pregnancy to 4 months postpartum, Chu et al. (2019) found persistent changes in knee laxity. Results indicated reduced laxity and compliance in the varus and posterior directions and increases in anterior compliance (Chu et al., 2019). Based on these and similar findings, pregnant women and women within 12 months postpartum are often excluded from biomechanical studies of GJH (Alsiri et al., 2020a; Rombaut, Malfait, De Wandele, et al., 2011).

4.6 Physical Activity and Exercise

Physical activity and exercise widely for those with GJH, from sedentary to high level athletes. Physical activity is bodily movement done at work, home, for transportation or during leisure time (Maddison et al., 2007). Exercise is category of physical activity that is planned, structured, repetitive and purposeful with the goal of improving physical fitness and/or health (Dasso, 2019). The association of

volume of physical activity or exercise and GJH-related joint trauma has not been studied. Level of physical activity is not always measured in studies of non-athlete populations with GJH and measures are not standardized. To et al. (2019) found no difference between overall score in physical activity between control and symptomatic using the IPAQ but, with a sample size of 24, greater certainty in the results could be determined by reproducing the study. Overall, it seems that adults with GJH have diminished levels of regular physical activity and significantly lower sport participation compared to those without GJH (Rombaut, Malfait, et al., 2010). Common barriers to physical activity in those with symptomatic GJH are pain, fatigue and fear of injury (Simmonds et al., 2019). Exercise, particularly proprioceptive and muscular strength training, is a key component in GJH treatment improving quality of life and function (Buryk-Iggers et al., 2022; Engelbert et al., 2017; Simmonds et al., 2019).

In those who exercise, risk of injury may be increased with presence of GJH. In university students aged 19-25 who were regularly physically active (2 or more fitness activities per week), the risk of injuries was related to diagnosed GJH ($BS \geq 4$) and pain threshold in lower limbs (Sieńko-Awierianów & Chudecka, 2020). For athletes with GJH, for whom hypermobility may provide a performance advantage, meta-analyses show increased injury risk for knee but not the ankle in contact sports and that athletes with GJH are three times more likely of having shoulder injuries than athletes without GJH (Liaghat et al., 2021; Pacey et al., 2010). In a study of 36 professional dancers with the same level of training, GJH ($BS \geq 4$) was related to lower levels of physical fitness, and higher levels of fatigue, musculoskeletal complaints and psychological distress (Scheper et al., 2013). The role of physical activity in mediating GJH, particularly in non-athletes with different levels and types of physical activity, has yet to be fully investigated.

4.7 Joint Instability

Joint instability and hypermobility may be related, but the presence of one of these features does not ensure the presence of the other. Joint instability is the inability to control, maintain or return to proper joint alignment. Static joint stability is impacted by the joint capsule, muscles, tendons, ligaments,

cartilage and bone articulation. Dynamic joint stability is a complimentary interaction between static components of joint stability, the sensorimotor system and neuromuscular control (Sell & Lephart, 2010; Wikstrom et al., 2006). Hypermobility refers to the ability of a joint move beyond normally expected ROM. Both hypermobility and instability describe a lack of joint support that increase the risk of micro- and macro-traumas and soft tissue degeneration. While joint instability infers a current or future joint pathology, JH may be benign or pathological. JH is one of many causes of joint instability which can also include muscular disorders, neural dysfunction and/or congenital or acquired musculoskeletal abnormalities (Castori et al., 2017). Currently, there are no studies addressing the interaction between stability/instability and non-GJH/GJH but the presence of joint instability, regardless of its cause, increases likelihood of articular pain and/or injury.

5 Biomechanics of Joint Hypermobility

5.1 Postural Control

People with symptomatic GJH have impaired balance and postural control. Symptomatic GJH groups show increased COP excursion (measured as COP distance and standard deviation of COP distance) during single leg balance with eyes open and eyes closed and increased anteroposterior sway during prolonged standing compared to non-GJH controls (Bates et al., 2021c; Galli, Rigoldi, et al., 2011; Iatridou et al., 2014; Rombaut, Malfait, De Wandele, et al., 2011). Rombaut et al. (2011) also found that those with symptomatic GJH had greater standard deviation of COP excursion and sway area during the Tandem Step test, a measure of fall risk, and the Modified Clinical Test of Sensory Interaction on Balance (mCTSIB), a measure of postural control under different sensory conditions. Iatridou et al. (2014) found greater mediolateral and anteroposterior deviation from COP mean with eyes open and head extended, and increased number of landing errors during a single leg hop test in the symptomatic GJH versus non-GJH group. In response to a series of six sudden forward perturbations, those with symptomatic GJH had significantly higher cumulative joint angle in the hip and knee (cumulative sum of change in angle) in first two perturbations than those with asymptomatic GJH and controls. Compared to non-GJH, those with GJH were able to normalize their muscular response but not cumulative joint angle over the six perturbations, which may indicate impaired balance control and reduced postural stability. It may also indicate a learned response to repeated perturbations (Bates et al., 2021a).

5.2 Gait

The only common findings in gait studies of symptomatic GJH compared to non-GJH groups are reduced step length, (Alsiri et al., 2020a; Bates et al., 2021b; Galli, Cimolin, et al., 2011; Rombaut, Malfait, De Wandele, et al., 2011), reduced stride length (Alsiri et al., 2020a; Bates et al., 2021b; Rombaut, Malfait, De Wandele, et al., 2011) and reduced gait velocity (Alsiri et al., 2020a; Bates et al., 2021b; Robbins et al., 2020). A 2015 meta-analysis on gait kinematics and kinetics included 6 studies and 146 participants and found no evidence that gait differs between GJH and non-GJH groups (Bates &

Alexander, 2015). Comparing results is difficult due to heterogeneity of outcome measures, methods, differences in groups tested (symptomatic versus asymptomatic), age (children versus adults), low statistical power, large number of outcomes measured, possible data-dredging, and potential for confounding factors like pain affected results. Bates & Alexander (2015) point out that of the 67 outcome measures in the five papers (sample sizes from 12 to 29) included in their meta-analysis, no single outcome measure was shared across all five the papers. Four papers included peak knee extension and three papers included knee flexion at heel strike. Further, of the common outcome measures, the results between studies were conflicting (Bates & Alexander, 2015).

Published studies on gait since 2015 have not yielded any further clarity regarding the inconsistent findings around gait and GJH identified by Bates & Alexander (2015). Alsiri et al. (2020b) compared a 10m overground gait in adults with symptomatic GJH ($BS \geq 4$) and non-GJH ($BS \leq 4$) and found the GJH group had decreased stride length, walking speed and step length, increased stance and double support phase and less knee flexion in swing phase compared to control. The JHS group also showed reductions in hip extension and knee power generation (Alsiri et al., 2020a), findings which were not reproduced by Bates et al. (2021c). Bates et al. (2021c) found no difference in overground gait kinematics between symptomatic GJH, asymptomatic GJH and non-GJH groups. In 6m gait trials, those with symptomatic GJH had lower moments and generated less power in the ankle and favoured power generation at the knee in the sagittal plane (Bates et al., 2021b). (Bates et al., 2021b). Comparing groups with and without EDS, Robbins et al (2020) found decreased step length, gait speed and longer time in stance phase but no difference in joint angles. The EDS group also showed significantly different muscle activation during gait (Robbins et al., 2020).

There are mixed findings in three studies on treadmill walking. Zhong et al. (2021) and Zeng et al. (2023) investigated knee kinematics of university-aged subjects (18-22 years old) during treadmill walking. Neither author makes clear if the GJH group was symptomatic or asymptomatic and pain was not measured. Zhong et al. (2021) reported greater active anterior/posterior translation, greater flexion in

the terminal stance and greater anterior tibial translation in the GJH ($BS \geq 4$). The length of treadmill walking was not reported and only Ball et al. (2024) mentioned fatigue as a potential confounder (Zeng et al., 2023; Zhong et al., 2021). Zeng et al. (2023) examined the effect of knee hyperextensibility (as assessed by the BS) on gait. Results showed those with GJH, but without knee hyperextensibility, had greater knee flexion angles and anterior tibial translations than those with GJH with knee hyperextensibility. When compared to controls ($BS = 0$), those with GJH without knee hyperextensibility showed greater anterior tibial translation and those with GJH without knee hyperextensibility showed increased extension angle (Zeng et al., 2023). Ball et al. (2024) investigated ankle, knee and hip kinetics and kinematics during gait in the dominant leg in age and sex matched groups with and without hEDS ($n = 11$, age = 36.4 ± 10.5 years; $n = 11$, age = 34.5 ± 15.5 years respectively) on an instrumented treadmill. No difference was found in kinematics. The hEDS group showed 37% lower peak hip extensor moment compared to the non-EDS group, which the authors suggest may be linked to lower hip extensor strength or the high incidence of hip subluxations in the hEDS group (73% reported hip subluxation at least once a week) (Ball et al., 2024).

Symptomatic GJH may be differentiated from non-GJH gait in inter-segmental variability and foot joint mobility. Robbins et al. (2022) investigated inter-segmental coordination (the phase/time-space relationship between segment pairs) as a measure of motor coordination in adults with and without EDS. Results showed greater inter-segmental coordination variability (over five gait trials) for the foot-shank and shank-thigh pairs in the sagittal plane during stance and swing phase and for the foot-shanks pair in the frontal plane during stance phase (Robbins et al., 2022). No difference in inter-joint variability was found between children with and without HSD (Jeong et al., 2024), which may reflect age or disease progression or the differences in symptoms in HSD and EDS (musculoskeletal versus multi-systemic). Vermeulen et al. (2022) found increased pain, foot dysfunction and hypermobility throughout the foot, particular at the first ray (first metatarsal and first cuneiform bones). Foot hypermobility was identified during gait using multi-segment ankle and foot (Ghent). Those with hEDS/HSD showed increased

eversion of the medial forefoot, more dorsiflexion in the medial and lateral forefoot and rearfoot, increased plantarflexion at midfoot, and decreased dorsiflexion and increased inversion and abduction at the hallux (Vermeulen et al., 2022). Identifying functional hypermobility in kinematic analysis may require modelling techniques that reflects these significant results.

5.3 Stair Climbing

Muscle activation during stair use appears unique in GJH. Luder et al. (2015) found altered movement patterns in females 18-40 years old ($n = 195$) with GJH ($BS \geq 6$, hypermobile right knee) to an age and sex matched group without GJH. Compared to people without GJH, during the ascent phase, those with GJH showed lower magnitude quadriceps activity and, in the descent phase, those with GJH showed lower magnitude quadriceps and hamstrings activity. The authors suggested that the small differences seen between groups may be due to the low demand of the task (Luder et al., 2015). Increased mean hip angle during stair ascent and descent and decreased power at the ankle has been noted in symptomatic GJH (Bates et al., 2021b). Bates et al. (2021b) found that during stair climbing and gait the clearest differences were between non-GJH and symptomatic GJH, with little difference between asymptomatic GJH and the other two groups in hip and ankle power and hip angle. The authors suggested that their results may represent at a spectrum of kinematic and kinetic characteristics from non-GJH to symptomatic GJH with asymptomatic GJH in between (Bates et al., 2021b).

5.4 Vertical Jump

Higher demand activities did not appear to reveal meaningful difference between those with and without GJH. Alsiri et al. (2020a) selected a vertical jump as a task, hypothesizing that the greater demand of this task would reveal greater differences between symptomatic GJH ($BS \geq 4$) and controls ($BS \leq 4$). However, no statistical difference between kinematics and jump heights was found. There was a statistical difference in lower knee and ankle peak moments during the compression phase and lower sagittal hip and knee peak power generation during the push phase but was deemed not clinically relevant based on a standardized mean difference of < 0.05 (Alsiri et al., 2020b). Examining asymptomatic GJH

group and control groups aged 19-25, Ewertowska et al. (2020) found no difference in counter movement jump height between groups.

5.5 Compensatory Strategies

5.5.1 Muscle Activation

Muscle activation in those with GJH is different from those without GJH. There are several possible mechanisms underlying these differences including stabilizing joints, reduced proprioception, poorer balance, reduced strength and the presence of symptoms. Knee stabilization strategies in GJH have been identified as reduced muscle activation in the hamstring during isometric knee flexion (Jensen et al., 2013), lower gastrocnemius during gait (Schmid et al., 2013) and quadriceps during stair climbing (Luder et al., 2015). During gait, Robbins et al. (2020) showed that those with EDS had lower hip and ankle strength and differences in muscle activation including: delayed vastus lateralis and medialis, higher rectus femoris and tensor fascia late, prolong gluteus medius and lower medial gastrocnemius activation. The authors suggested that muscle activation patterns were a result of reduced proprioception, poorer balance and decreased strength in hip and ankles (Robbins et al., 2020).

Muscle activation in those with GJH may differ based on BS and presence of symptoms. In a group with GJH, those with higher BS displayed greater decreased torque steadiness and knee flexor coactivation than the non-GJH group (Jensen et al., 2013). During isometric contraction (single leg knee extension), significantly higher rate of force development was recorded in symptomatic and asymptomatic women with GJH ($BS \geq 6$) compared to those without GJH ($BS \leq 1$) (Mebes et al., 2008) and lower peak hip extensor strength in age and sex matched controls with and without hEDS (Ball et al., 2024). Luder et al. (2015) found the differences between those with and without GJH in stair climbing were augmented with symptomatic GJH and proposed possible explanations could include pain-related muscle inhibition, avoidance of higher muscle activation and higher joint contact forces. Clearer differences in muscle activation patterns may require more challenging activities and/or fatigue-inducing movements (Luder et al., 2015).

5.5.2 Reduced Range of Motion

While those with GJH have larger than expected ROM in several joints during the BS, they can demonstrate smaller than expected ROM during dynamic tasks. Alsiri et al. (2020a, 2020b) proposed the theory that the lack of differences between GJH and control groups was due to a “stiffening” pattern (characterized by reduced ROM) that allowed hypermobile joints move in non-hypermobile ROM during walking and vertical jumps. In terms of gait, reduced ROM was seen in both kinematics in the slight reduction in knee flexion in swing phase and clinically, but not statistically and clinically relevant reductions, in pelvic upward obliquity and hip abduction, and kinetics, reductions in hip extensor moment and knee power generation (Alsiri et al., 2020a). During vertical jumping, there no difference in ROM between GJH and non-GJH, and there were statistically significant, but not clinically relevant, reductions in hip and knee peak power and ankle and knee peak moments in the GJH group (Alsiri et al., 2020b). While this theory is called “stiffening” by the authors, they are referring to reduced ROM only, and not joint stiffness.

5.5.3 Dynamic Knee Joint Stiffness

Knee joint stiffness in GJH has not been studied. Dynamic knee joint stiffness (DKS) is defined as the ability of the active (muscles and tendons) and passive articular soft tissue (ligaments) to resist an applied moment (Davis & DeLuca, 1996). DKS is the slope of the line when moment is plotted against angle. In other clinical populations, DKS is generally measured during gait. Gustafson et al. (2016) showed that in people with knee OA, those with knee instability had significantly lower stiffness those with stable knee. Additionally, regression analysis showed that walking knee stiffness was not associated with common OA-related risk factors (quadriceps weakness, passive medial compartment joint laxity and varus knee malalignment) (Gustafson et al., 2016).

Unlike many other gait parameters, DKS is unrelated to walking speed. Except for knee joint excursion, differences in gait parameters (knee and ankle joint moment, ground reaction forces, knee reaction force and knee excursion) between those with knee OA and healthy controls have been

accounted for by self-selected walking speed (Zeni & Higginson, 2009a). However, when measuring DKS, differences were found at 1.0 m/s, self-selected and fast walking speeds between a group with severe knee OA and groups with moderate knee OA and healthy controls. For OA and healthy groups, DKS increased with walking speed (Zeni & Higginson, 2009b).

It is possible that, similar to knee instability and several gait parameters, GJH may be related to DKS. Measuring DKS may be sensitive to differences between GJH and non-GJH joints that are obscured by compensatory strategies during static and dynamic tasks. Of the movements reviewed above, tests of balance yield the most consistent and clearest findings in GJH samples. Finding a task more challenging than single leg balance and a task more novel than gait or stair climbing, for which compensatory strategies have not been formed, may be even more information in distinguishing between GJH and non-GJH groups.

6 Dynamic Balance: Modified Star Excursion Balance Test

The modified Star Excursion Balance Test (mSEBT) is a reliable, non-instrumented clinical test for assessing lower limb dynamic balance and lower extremity function (Gribble et al., 2012; Picot et al., 2021; Powden et al., 2019). While the terms dynamic postural control (maintaining or restoring centre of mass within the base of support during movement and in response to perturbations) dynamic postural stability (maintaining balance while going from a dynamic to static state) and dynamic balance can have different meanings they are both used to describe the mSEBT task (Gribble et al., 2012; Karagiannakis et al., 2020; Petter et al., 2022; Picot et al., 2021; Pollock et al., 2000; Wikstrom et al., 2005). This study uses the term dynamic balance to identify the task being assessed by the mSEBT. Dynamic balance is defined as maintaining centre of mass within the base of support while intentionally creating body movement away from the base of support. Dynamic balance activities are distinct from static balance activities because they more closely reflect the demands of functional activities (Gribble et al., 2012).

Task. The mSEBT involves establishing a stance limb at the base of support at the centre of a testing grid while the other limb reaches in three directions (anterior, posterolateral and posteromedial). The outcome measure is the reach distance of the non-stance leg in each direction. Maximum reach distance (MRD), calculated as composite score of the average of all directions, is used index of dynamic balance. The farther the MRD, the better dynamic postural control and balance. MRD can be used to measure changes in dynamic balance within subjects (e.g., pre- and post- treatment or surgery) and when the values are normalized to limb length, can be used as an objective measure of deficits in dynamic balance and may help evaluate risk of lower limb injury (Gribble et al., 2012; Picot et al., 2021). In the case of a GJH population, the mSEBT could indicate deficits in dynamic balance in the stance leg that is required to maintain stability during the reach tasks.

Validity and reliability. The SEBT produces data that is valid in identifying dynamic balance deficits for those with lower extremity conditions, predicting lower extremity injury risk, and measuring changes in training programs for lower extremity conditions. It is a “highly representative, non-

instrumented dynamic balance test for physically active adults” (Gribble et al., 2012). Validity of the SEBT and mSEBT are considered the same when appropriate testing protocols are followed (Picot et al., 2021). The mSEBT produces data with excellent inter- and intra-rater reliability. For the anterior, posteromedial and posterolateral directions respectively, median ICC for inter-rater reliability values were 0.88, 0.87 and 0.88 and for intra-reliability median ICC values were 0.88, 0.99 and 0.90 (Picot et al., 2021).

Key to the validity and reliability of the mSEBT is following guidelines for testing procedures and interpretation. As of 2021, practical guidelines suggested using the three-direction mSEBT instead of the eight direction SEBT to avoid redundant testing while maintaining test reliability. Updated recommendation are described for mSEBT/SEBT procedures on number of directions, test set up, familiarization trials, recorded trials, hand and foot position, failure/success criteria, measurement parameters and limb length normalization (Picot et al., 2021). mSEBT guidelines also provide a list of intrinsic factors that affect the between subject comparisons of the mSEBT/SEBT, which are explored in section 6.2.

6.1 Biomechanics of the Modified Star Excursion Balance Test

6.1.1 Kinematics, Kinetics and Balance

Kinematics, kinetics and balance control affect performance on the mSEBT. Overall, better performance on the SEBT in healthy individuals is achieved through greater knee flexion, hip flexion or both knee and hip flexion (Robinson & Gribble, 2008). When comparing bilateral asymmetry in MRD within an individual, performance depends on the direction of movement away from the BOS. Balance plays the greatest role in the anterior direction; greater COP area and maximum anterior-posterior COP excursion are associated with greater MRD (Ortega et al., 2020; Petter et al., 2022). In the posteromedial reach direction, joint moments best predict differences; greater ankle adduction internal moment and right ankle axial moment are associated with greater MRD. In the posterolateral direction, kinematics are the

best predictors of MRD, but knee, hip and ankle kinematics vary between individuals (Ortega et al., 2020).

6.1.2 Surface

Uneven surfaces provide an additional challenge in dynamic balance tasks. Foam, an accessible way to alter the support surface, in clinical and research settings, increases postural sway velocity during standing (Gosselin & Fagan, 2015). In foam and no foam conditions in 20 healthy participants (10 males, 10 females, aged 20-27) Nozu et al. (2021) measured the posteromedial reach of the mSEBT and found significant differences in ankle, knee, hip and trunk kinematics. The greatest differences between foam and no foam conditions were in the knee, MRD, and COM and COP position and displacement. In the foam condition, there was greater knee flexion, hip flexion and knee varus. There were significant interaction effects between surface condition and ankle dorsiflexion, ankle rotation and trunk flexion. Greater ankle dorsiflexion and trunk flexion was observed at the beginning and last 10% of each reach on foam versus no foam. Participants reached farther without foam than with foam (mean difference = 4.58%; 95% CI [3.50, 5.66]). On the foam, center of mass and COP of the stance limb were more lateral during the reach task and more anterior during standing (Nozu et al., 2021). In collegiate athletes and recreationally active subjects, Sabin et al. (2010) found greater reach distance in a modified mSEBT on stable versus unstable surfaces in the medial (4.5% further) and posterior (9% further) directions and in the average of all three directions (5% further) (Sabin et al., 2010).

6.2 Intrinsic Factors Influencing Performance on the mSEBT

6.2.1 Sex

There may be connection between sex, knee angle and MRD, though these associations are not consistent. In a study of healthy subjects, females had better postural control and tended to score better (higher MRD) than males and use an average of 4° knee flexion in the anterior direction and 5° more knee flexion in the posterior direction compared with males (Gribble et al., 2009, 2012). Nonetheless,

normalization of MRD to leg length attenuated sex differences (Gribble et al., 2012; Picot et al., 2021), suggesting the influence of anthropometrics.

6.2.2 Foot Type

Most studies find no influence of foot type when using the mSEBT/SEBT as an outcome measure. Among the studies who found a difference, it was negligible, and no clear differences have been found between foot types (Gribble et al., 2012; Picot et al., 2021).

6.2.3 Limb Dominance

There is no evidence of influence of limb dominance in healthy adults or athletes (Picot et al., 2021).

6.2.4 Age and Level of Play

When comparing high school and university athletes, older individuals playing at a higher level score better normalized scores in the posterolateral and posteromedial directions and in the composite score than those that are younger and at lower level of play (McCann et al., 2015; Picot et al., 2021). Recreationally active subjects (3-4 fitness activities/week) showed higher MRD than collegiate basketball players in anterior, medial and posterior reach directions (Sabin et al., 2010). Sabin et al. (2010) suggest that basketball-specific training and demands, when compared to the control group, could explain these unexpected results.

6.2.5 Type of Sport

Normalized SEBT scores vary across sports. In a study of 12 university-level sports teams and 7 sports, there were differences in normalized MRD between sports (range across all teams = 82.1% - 96.6%) (Stiffler et al., 2015). Comparing male and female teams showed a sex-sport interaction for soccer, such that female soccer players demonstrated greater MRD scores compared to their male counterparts, particularly for soccer (Stiffler et al., 2015). Differences in SEBT performance between sports may depend more on unique sensory motor challenges of reaching task rather than general athletic

training. For example, soccer players show higher MRD versus basketball players (Bressel et al., 2007). There is no published literature on the effect of prior or childhood balance training in SEBT or mSEBT scores. However, Thai Khon Masked Dancers, a sport that emphasizes balance, aged 18-23 with 3-10 years of experience had greater MRD than age and sex matched non-dancers in the SEBT (Krityakiarana & Jongkamonwiwat, 2022).

6.2.6 Injury Status

Knee and ankle injury and surgery affect MRD. In the SEBT, chronic ankle instability results in reduced MRD in all directions and reduced “complexity of COP path” compared to controls and reduced MRD in the posterolateral direction compared to lateral ankle sprain copers (Doherty et al., 2016). Chronic ankle instability (CAI) also results in different hip and ankle angles and trunk displacement than controls; though angles have been measured as both higher and lower than non-CAI controls (Doherty et al., 2016; Hoch et al., 2016). MRD in the anterior direction is lower for those post anterior cruciate ligament reconstruction surgery compared to uninjured controls (Clagg et al., 2015).

6.2.7 Fatigue

Among healthy, physically active young adults (aged 19-35), Gribble et al. (2009) showed that fatigue augmented differences in MRD between female and male participants.

6.2.8 Patellofemoral Pain

Those with patellofemoral pain syndrome (PFPS) have shorter MRDs than those without PFPS (Gribble et al., 2012).

7 Knowledge Gaps

A critically important need for those with symptomatic hypermobility is accurate, easily accessible diagnosis. To meet this need, a diagnostic test that is quick and easy to use, that also produces valid and reliable data may help decrease diagnostic delay.

1. The mSEBT has not yet been studied in GJH groups. There is potential that this clinical test, which is already in widespread clinical use to document dynamic balance, could be useful to identify GJH. There may be additional benefits of using this dynamic balance test to understand the functional implications of GJH, which may produce indications for rehabilitative strategies that could augment patient care and improve quality of life. In addition to categorization by mSEBT score, quantification of performance on the mSEBT may allow identification of individuals with asymptomatic GJH who are at risk for developing symptoms.

2. There are gaps in understanding the biomechanical implications of hypermobility in lower extremity joints. There is a clear difference seen in postural stability between GJH and non-GJH groups, however, there are mixed results regarding impacts of GJH on gait, stair climbing and vertical jumps. There seems to be some difference in muscle activation patterns compared to control groups. Characterizing the biomechanics of GJH may require better diagnostic criteria and testing and/or using novel tasks or conditions.

3. Biomechanical testing of GJH has been conducted with custom, research-grade equipment (e.g., force plates) for studies of postural stability and perturbations, and/or use outcome measures requiring equipment that is not feasible for clinical use. However, there is some potential that simple tools, such as foam to alter terrain, could prove useful in identifying GJH. Those with symptomatic hypermobility find it more difficult to move on unstable surfaces than those without hypermobility (Palmer et al., 2020). While no studies have incorporated unstable surfaces and functional movements, it is possible that unstable surfaces may elicit greater differences between GJH and non-GJH joints in

functional tasks and/or widely used, easy to implement, accessible clinical assessments of function, injury risk and/or dynamic balance.

4. Currently, there is no data on the incidence of joint instability (the inability to control, maintain or return to proper joint alignment) in GJH or on the effects of stable versus unstable hypermobile joints and the possible impact on symptoms and function. Joint instability can arise from multiple causes, both acquired and congenital, and hypermobility may be present with or without instability. It is not yet known if there is a relationship between symptomatic JH, early joint degeneration and instability. Investigating a hypermobility-instability connection will likely require a modeling approach, which is beyond the scope of this project. Such work would require more data about hypermobile soft tissue mechanics and/or dynamic systems of hypermobile populations, the latter of which this study could provide.

5. Dynamic knee joint stiffness has not been studied in individuals with GJH. Given the relationship between joint stiffness and knee instability, as well as the difficulties in capturing knee instability directly, DKS may give some insight into the possible differences in active and passive soft-tissue contribution to dynamic knee function in those with and without GJH.

8 Purpose

The overall purpose of this study was to test whether performance of a dynamic balance test, the modified Star Excursion Balance Test (mSEBT), on stable and unstable surfaces, distinguishes between GJH and non-GJH in age matched adults. In addition to the maximum reach distance score traditionally derived from the mSEBT, performance was also measured using lower limb kinematics end excursion of the centre of pressure beneath his standing foot. A secondary purpose was to compare dynamic knee stiffness (DKS) in adults with and without GJH and non-GJH groups. Finally, this study determined the associations of performance on the mSEBT with (i) the diagnostic criteria (BS) and (ii) a validated clinical measure of disease impact. The findings contribute 3 novel approaches. First, I explore the utility of a common clinical and accessible dynamic balance test and identifying GJH. Second, I contribute new data on joint biomechanics in GJH. Third, I explore the association of dynamic balance with disease impact in DJH.

8.1 Primary Objectives

The primary objective was to compare performance during the mSEBT, a weight-bearing dynamic balance task, in stable, unstable and timed conditions in adults with and without GJH. During the mSEBT, performance was measured using maximum reach distance, maximum knee joint angle and total excursion of the centre of pressure.

8.2 Secondary Objectives

There were two secondary objectives. One secondary objective was to compare DKS during gait in adults with and without GJH. Another secondary objective was to determine the associations of performance on a dynamic balance task with (i) the current diagnostic criteria and (ii) measure of disease impact.

8.3 Hypotheses

Regarding the primary objective, it was hypothesized that there would be a difference between GJH and non-GJH groups in maximum reach distance, maximum knee joint angle and COP total excursion. Previous research showed reduced postural stability in people with GJH compared with healthy controls and an association between shorter maximum reach distance and lesser maximum knee flexion angle (Nozu et al., 2021; Rombaut, Malfait, De Wandele, et al., 2011). Therefore, it was expected that maximum reach distance and maximum knee joint angle would be smaller and COP total excursion would be greater in a GJH group versus a non-GJH group, with these between-group differences being greatest in the unstable condition.

Regarding the secondary objectives, it was hypothesized that there would be a difference between groups in DKS. Based on previous research which showed lower dynamic ankle stiffness in GJH compared with healthy controls (Rigoldi et al., 2012), it was expected that DKS would be lower in the GJH group (the GJH group would be “less stiff”). Previous research demonstrated that a measure of disease impact, the BIoH, is a valid tool to differentiate between symptomatic GJH and non-GJH groups and that the BS is not a valid measure of GJH (Malek et al., 2021; Palmer et al., 2020). Therefore, it was also hypothesized that there would be a stronger association between mSEBT performance with the measure of disease impact of GJH than the current diagnostic criteria.

9 Methodology

9.1 Study Design

This study was a cross-sectional design comparing two groups (GJH and non-GJH) performing the mSEBT in three conditions: stable (no foam surface), unstable (foam surface) and stable and timed; as well as overground gait on a level surface. It involved a single testing session which included participants completing self-report questionnaires (BLoH, pain, physical activity), Beighton Score, leg dominance testing and bilateral motion analyses during mSEBT and gait (Figure 1).

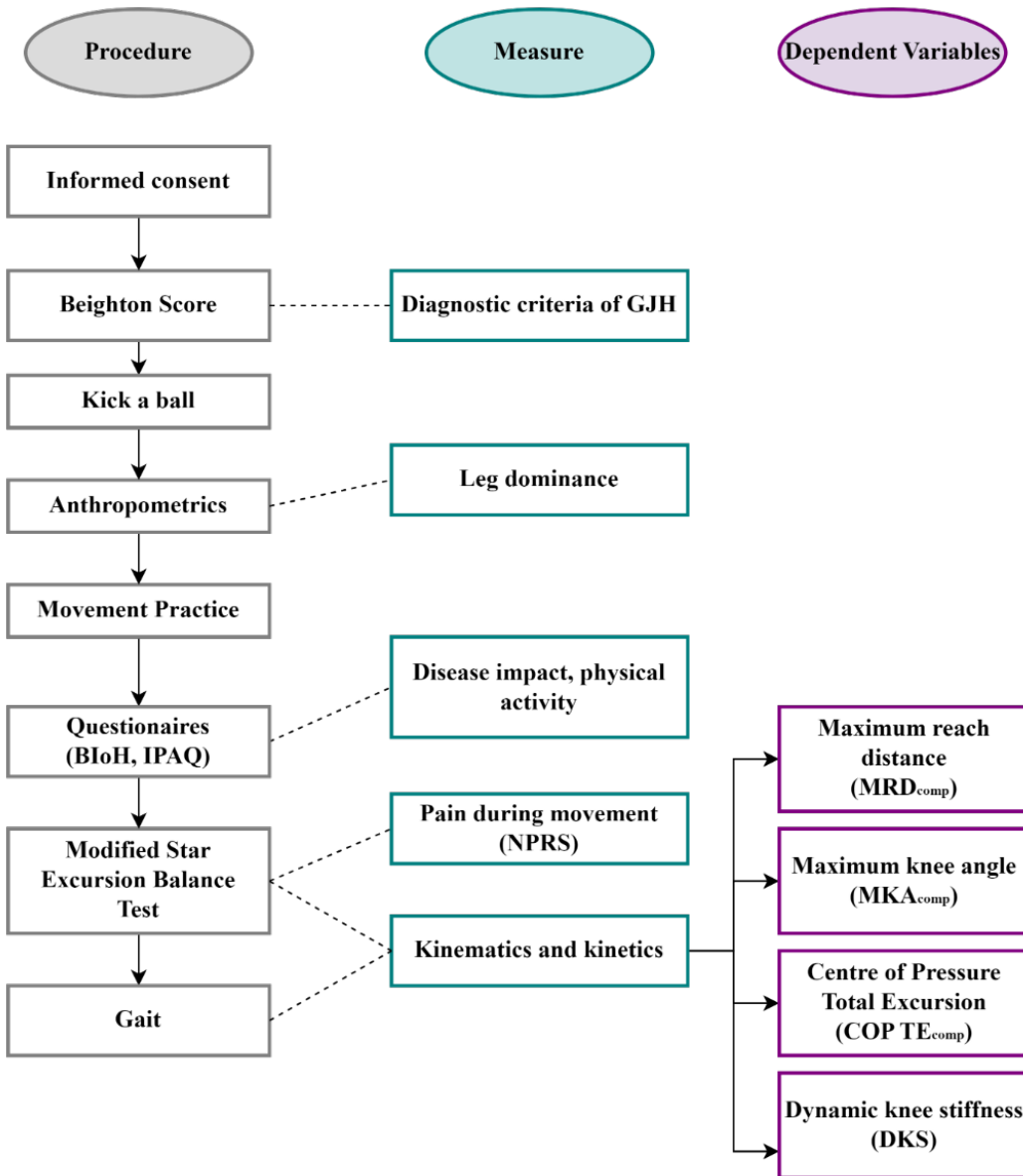


Figure 1. Visual representation of study protocol and associated measures. BloH = Bristol Impact of Hypermobility Questionnaire; GJH = Generalized Joint Hypermobility; IPAQ = International Physical Activity Questionnaire; NPRS = Numeric Pain Rating Scale.

9.2 Participants

9.2.1 Inclusion Criteria

Participants were aged 18-38 years old and split into two groups: one non-GJH group (BS <5) and one GJH group (BS ≥5). Participants in these two groups were matched by age (± 3 years from month and year of birth) and stratified by sex.

9.2.2 Exclusion Criteria

Potential participants in both the GJH group and non-GJH groups were excluded for the following criteria:

- Surgery in joints assessed within the BS (spine, knees, elbows first and fifth metacarpals) as well as the ankle.
- Diagnosis of a heritable connective tissue disorder other than hEDS.
- History of ankle sprain (Doherty et al., 2016) that required intervention.
- A pathological neurological, vestibular or visual condition that could impair motor performance in dynamic balance tasks.
- Current competitive athletes (McCann et al., 2015).
- Current physical activity greater than 4 fitness activities (30 minutes or more of structured exercise, e.g., cardiovascular, strength, or balance training, sporting activities) per week (Bressel et al., 2007; Sabin et al., 2010)
- Current single leg balance training.
- Pregnant or fewer than 12 months post-partum (Opala-Berdzik et al., 2018).
- Patellofemoral pain syndrome.
- Other health conditions that can cause multiple joint pain (fibromyalgia, rheumatoid arthritis) (Palmer et al., 2020).

In the non-GJH group, participants were excluded if they had any current or chronic lower extremity joint pain.

9.2.3 Recruitment Strategy

Recruitment occurred in cycles of two stages. In the first stage, recruitment focused on identifying potential participants with GJH in blocks of 5 individuals. In the second stage, recruitment identified age-matched potential participants for the non-GJH group. A cycle of the first and second stages continued until sample size was reached.

Participants were recruited at the University of Waterloo and in the Waterloo community using multiple strategies: (1) Recruitment posters were placed in libraries, food halls, and student lounges. (2) Wherever possible, recruitment information was distributed to large lecture classes for non-kinesiology majors (e.g., HEALTH 100/105). An effort was made to recruit participants from non-kinesiology departments (e.g., English and Engineering) by asking undergraduate/graduate coordinators to distribute recruitment information within their departments. Non-kinesiology programs were included in recruitment to avoid over-sampling physically active participants. (3) Community recruitment was done through social media (e.g., Department X account). After contacting the student researcher, potential participants were screened for eligibility in person or via e-mail based on exclusion and inclusion criteria and separated into group using the 5PQ. The 5PQ is a quick, self-reported questionnaire consisting of five yes or no questions (Figure 2; Appendix C). Answering “yes” to two or more out of five questions suggests likely symptomatic GJH with 84% sensitivity and 80-89% specificity (Hakim & Grahame, 2003; Malfait et al., 2017).

	Yes	No
1. Can you now (or could you ever) place your hands flat on the floor without bending your knees?		
2. Can you now (or could you ever) bend your thumb to touch your forearm?		
3. As a child, did you amuse your friends by controlling your body into strange shapes or could you do the splits?		

4. As a child or teenager, did your shoulder or kneecap dislocate on more than one occasion?		
5. Do you consider yourself double-jointed?		

Figure 2. Five-Part Questionnaire for Identifying Hypermobility (5PQ). Answering “yes” to 2 or more suggests symptomatic JH with 84% sensitivity and 80-89% specificity. The 5PQ is also used to diagnosis historical HSD.

9.2.4 Sample Size Estimation

Many of the published studies on hypermobility, even those with access to patient populations, have sample sizes under 30. Often, due to the rarity of symptomatic GJH participants, matching on age and sex is not possible. No effect sizes are available for GJH in meta analyses. Effect sizes for symptomatic GJH versus control groups were calculated by Alsiri et al. (2020) from available published data. From the reduction in step length observed by Galli et al. (2011) (GJH n=10; non-GJH n=20) the effect size for spatiotemporal parameters was 0.84. Effect size for kinematic parameters based on a gait study which found a difference in ankle dorsiflexion in symptomatic GJH was 0.74 (Rigoldi et al., 2012) (GJH n = 12; Down Syndrome n=16; non-GJH = 20) . For kinetic parameters, the effect size was 0.70 during terminal stance based on Galli et al. (2011). Although given as only “effect size” in Alsiri et al. (2020) it is assumed, based on the a priori sample size of this study, these values represent Cohen’s d. Effect sizes for foam versus no foam conditions are $d = 1.15$ for knee flexion and $d = 1.63$ for knee varus (Nozu et al., 2021). The middle of these effect sizes was Cohen’s $d = 0.74$ was entered into G*Power 3.1 software (Heinrich Hein University, Dusseldorf, Germany) as 2X3 analysis of variance (ANOVA) with fixed/main effects and interactions with two groups and three measurements, an alpha of 0.05 (Type I error rate) and beta of 0.80 (Type II error rate). The estimation a sample of $n = 26$ per group with an actual power of 0.81.

Due to the scope of this project and the size of the GJH population who fit the exclusion criteria (particularly no history of ankle sprain and maximum 4 X 30 minutes of exercise per week), the a priori

target was a sample size of 30. Due to challenges recruiting participants matched on age and sex, 2 unmatched participants were collected for a total of 30 collections. Only matched participants (14 matched pairs) were used for data analysis.

9.3 Instrumentation

9.3.1 Kinematics

Three-dimensional kinematics were captured using a 5-camera bank (15 cameras) high-speed motion capture system (Optotrak Certus, Northern Digital Inc., Waterloo, ON, CA) sampled at 100Hz (Nozu et al., 2021). Rigid body clusters containing three infrared light emitting diodes (iRED) were attached to the superior sacrum, bilaterally on the mid-lateral thigh, mid-lateral shank, and anterolateral foot. Lower extremity rigid-link bodies for the thigh, shank and foot were created and defined using anatomical landmarks as defined in Table 2 (Robertson et al., 2014; Wu et al., 2002) from which a 7-segment rigid-link model was created for each participant. A standing calibration trial was used to transform the external markers of the 7 segments into a reference frame. For those with hypermobile knees, a plumb line was used to ensure that the standing calibration trial was recorded with knees in a neutral alignment (0° extension) so that accurate knee angles could be obtained (Figure 3). Neutral knee alignment was defined as: when the plumb line ran from the greater trochanter to the anterior edge of the lateral malleolus through the centre of the knee joint. Residual analysis for motion data was done on a foot marker during gait, which confirmed a cut-off frequency confirmed by other work (Bates et al., 2021b; Gustafson et al., 2016; Thomas et al., 2022; Zeni & Higginson, 2009a). Kinematics were filtered by a low-pass, dual-pass, fourth-order Butterworth filter with a 6 Hz cut-off frequency.

Table 2. Digitized marker number, anatomical locations and corresponding rigid body cluster for the foot, shank, thigh and pelvis segments. (L) = left, (R) = right.

Digitized Marker Number	Digitized Anatomical Landmark	Rigid Body Cluster
1	(L) Iliac Crest	Pelvis
2	(R) Iliac Crest	Pelvis
3	(L) Posterior Superior Iliac Spine	Pelvis

4	(R) Posterior Superior Iliac Spine	Pelvis
5	(L) Anterior Superior Iliac Spine	Pelvis
6	(R) Anterior Superior Iliac Spine	Pelvis
7	(L) Greater Trochanter	(L) Thigh
8	(L) Lateral Epicondyle	(L) Thigh
9	(L) Medial Epicondyle	(L) Thigh
10	(L) Fibular Head	(L) Shank
11	(L) Tibial Tuberosity	(L) Shank
12	(L) Lateral Malleolus	(L) Shank
13	(L) Medial Malleolus	(L) Shank
14	(L) Calcaneus	(L) Foot
15	(L) Dorsal Base of the 5 th Metatarsal Head	(L) Foot
16	(L) Dorsal Base of the 2 nd Metatarsal Head	(L) Foot
17	(L) Dorsal Base of the 1 st Metatarsal Head	(L) Foot
18	(L) Distal End of the 1 st Metatarsal	(L) Foot
19	(R) Greater Trochanter	(R) Thigh
20	(R) Lateral Epicondyle	(R) Thigh
21	(R) Medial Epicondyle	(R) Thigh
22	(R) Fibular Head	(R) Shank
23	(R) Tibial Tuberosity	(R) Shank
24	(R) Lateral Malleolus	(R) Shank
25	(R) Medial Malleolus	(R) Shank
26	(R) Calcaneus	(R) Foot
27	(R) Dorsal Base of the 5 th Metatarsal Head	(R) Foot
28	(R) Dorsal Base of the 2 nd Metatarsal Head	(R) Foot
29	(R) Dorsal Base of the 1 st Metatarsal Head	(R) Foot
30	(R) Distal End of the 1 st Metatarsal	(R) Foot

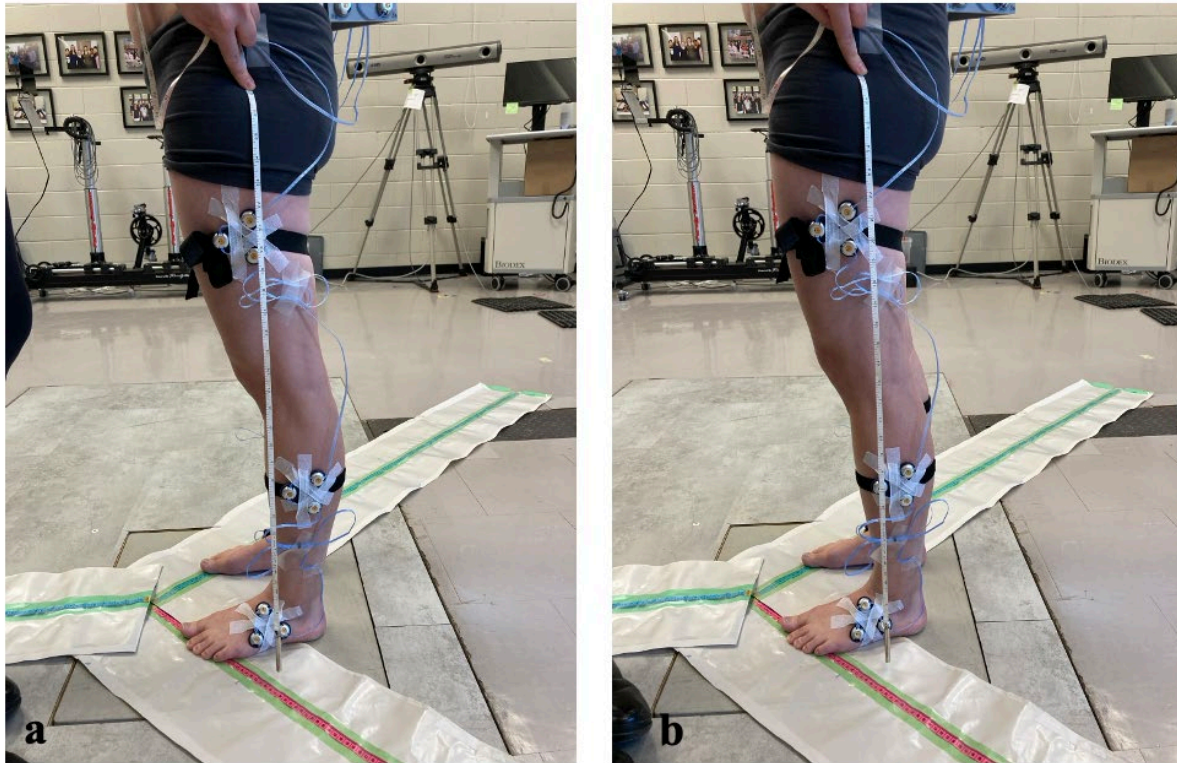


Figure 3. Set up for standing calibration trial in a neutral knee position for participants with hypermobile knees. A plumb line from the greater trochanters towards the floor was used to assess knee alignment. Neutral knee alignment was achieved when the plumb line ran from the greater trochanter to the anterior edge of the lateral malleolus through the center of the knee joint. Hypermobile participants were asked to slightly bend their knees until neutral alignment was achieved. **(a)** Lateral view of participant with hypermobile knees in their end range extension. **(b)** Lateral view participant with hypermobile knees in neutral alignment used for calibration trial.

Reliability and validity. Mazumder et al. (2007) demonstrated the high precision and excellent repeatability of kinematic data during gait collected using the Optotrak Certus. While dynamic balance has not been tested for reliability and validity, the mSEBT task is similar to gait in terms of the speed of movement and joint angles; thus, the reliability and validity of the Optotrak Certus was assumed to be similar for both tasks. In addition, using a robot that moved simultaneously in 3 dimensions, precision for the distance between markers was measured in static conditions (% error = 0.57, SD (mm) = 0.002-0.0043), dynamic conditions (% error = 0.57-0.58, SD (mm) = 0.0058-0.0086) and angles between markers in static conditions (% error = 4.01, SD (deg) = 0.00013-0.00019). Repeatability was assessed using a coefficient of multiple correlation (CMC). Constant speed had moderate repeatability (CMC =

0.63, SD (mm/s) = 0.26) and high repeatability was found in acceleration (CMC = 0.99, SD (mm/s) = 0.91), deceleration (CMC = 0.99, SD (mm/s) = 0.91), angle (CMC = 0.99, SD (deg) = 0.10), volume (CMC = 0.99, SD (m³) = 0.000015) and circular movement in x-axis (CMC = 0.99, SD (m) = 0.0094) and y-axis (CMC = 0.99, SD (m) = 0.0082) (Mazumder et al., 2007).

Assumptions and Limitations. Rigid-link modeling makes assumptions about the skeletal structure being represented. First, skeletal structures are assumed to be rigid bodies. For segments like the foot, which have many bones and joints, assuming rigidity is incorrect but was done to make mathematical calculations manageable and to help in the creation of a local coordinate systems (Robertson et al., 2014). Second, markers are assumed as fixed to the segment but are attached to the skin and, due the relative movement between skin and underlying bone (soft tissue artifact), there was error between the motion capture data and the movement of segments. This error was attenuated by the use of rigid clusters placed on segments and by the careful location of anatomical landmarks (Camomilla, 2017).

9.3.2 Kinetics

Kinetic data (ground reaction forces and centre of pressure) were collected synchronously with the motion capture system using a floor-embedded force plate (OR6-7, Advanced Mechanical Technologies Inc., Watertown, MA, USA) sampled at 1000Hz (Bates et al., 2021b). As indicated by a residual analysis and confirmed by previous work (Thomas et al., 2022), ground reaction forces were filtered with a low-pass, dual-pass, fourth-order Butterworth filter with a 10 Hz cut-off frequency. Kinetics were collected on both limbs.

9.4 Tasks

9.4.1 Modified Star Excursion Balance Test

The task protocol followed the 2021 updated recommendations for the mSEBT procedure by Picot et al. (2021). In clinical settings, the testing grid was a “Y” shape with three reach directions with anterior (ANT) at 0° with the posterolateral (PL) and posteromedial (PM) at 135° in each direction from

ANT (Figure 2a). The testing grid centre was also taped to the top of the foam pad so the pad could laid on top of the non-foam condition testing grid (Figure 2b).

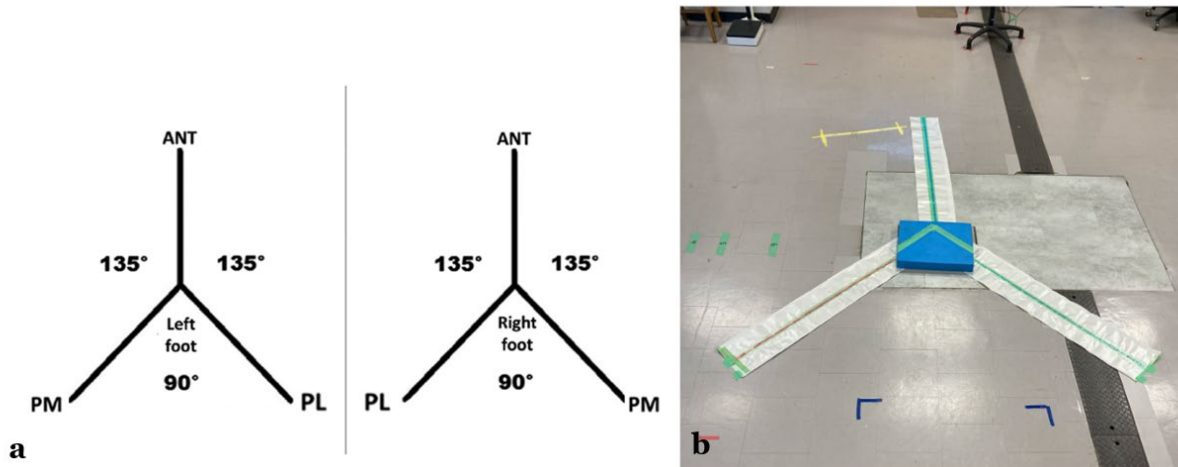


Figure 3. Modified Star Excursion Balance Test (mSEBT) testing grid with the centre placed at the crossing of the three lines. (a) Testing grid and angles from mSEBT guidelines (Picot et al., 2021), (b) Lab set up with the centre of the testing grid and foam placed over the inground force plate.

The experimenter explained the goal of the test, hand and foot placement and failure criteria. The goal of the test was to reach and then tap the distal end of the first metatarsal of the non-stance limb as far as possible along the test grid lines. Hands remained on the hips during test. The test was performed in barefoot. The distal end of the first metatarsal of the stance limb remained on the marked origin for the duration of the test. The return to double leg stance marked the end of each reach attempt. The following indicated a failed test: participant fell or lost their balance, weight shifted onto the reaching limb, the reaching limb contacted the floor more than once during a reach task or did not touch the grid lines, any part of the stance foot lifted or moved on the ground, and/or hands left the hips (Picot et al., 2021).

The participants were shown a live demonstration of the test by the experimenter. To avoid learning effects during testing, participants practiced at least four times in each direction for each limb to familiarize them with the procedure.

After a five-minute rest, four successful reach attempts were recorded for each direction in both conditions and legs for a total of 72 recorded reaches. Participants switched legs and rested for one minute between directions to minimize fatigue. The order of testing was randomized by assigning each reach direction, condition and starting leg (dominant or non-dominant) a number and using a randomizer.org to create 30 sets of 8 unique numbers. Each participant was assigned a set of numbers as their order of reach direction, condition order, and starting leg (Appendix G).

9.4.3 Conditions

During the mSEBT, participants were tested on the floor (timed and self-selected pace) and on a balance pad (Airex, Switzerland) used in previous studies of the mSEBT (Nozu et al., 2021; Sabin et al., 2010). The Airex balance pad is made of polyurethane (density = 38.6 kg/m³, thickness = 5cm). It deforms linearly up to 1320N (134.56kg) of applied force and produces the most uniform change in postural sway velocity over the largest range of participant mass compared with open-cell (urethane) and closed-cell foam pads (Gosselin & Fagan, 2015). During the timed condition participants were asked to perform each reach attempt in six seconds (three seconds to reach and tap and three seconds to return to double stance), guided by a metronome set to 60 BPM (Nozu et al., 2021).

9.4.4 mSEBT Measures

Maximum reach distance (cm) was defined as the maximum distance between the distal ends of the first metatarsals of the reaching and standing limbs during a successful reach. The distal end of the first metatarsal of the standing leg remained at the centre of the testing grid throughout the task. As per mSEBT guidelines, maximum reach was reported as a composite score (MRD_{comp} (%)): the mean of the three trials in each direction normalized to the length of the stance limb. Limb lengths were determined as the distance between the markers of the ASIS and medial malleolus in the standing trial (Picot et al., 2021).

Due to marker occlusion during the posteromedial and posterolateral reaches (when the dorsal surface of the foot was close to the floor) MRD_{comp} was measured in the following way: (i) the testing grid was affixed two pieces of paper which were covered with a wipeable plastic film; (ii) the grid was centered over the force plate and fixed to the floor/force plate (Figure 2); (iii) washable, non-toxic paint was placed on the distal end of the first metatarsal of the reaching limb; (iv) measurements were taken from the centre of the testing grid to the most distal part of the mark made by successful reach attempts. Benefits of this MRD measurement technique were its simplicity, similarity to clinical MRD measurement and biofeedback that may have encouraged participants to achieve their true maximum reach. Drawbacks of this technique included the experimenter choosing where on the painted mark to measure from. This disadvantage and the measurement error associated with it was attenuated by standardizing measurements (to the most distal edge of the paint mark).

Maximum knee joint angle ($^{\circ}$) was the maximum knee flexion angle achieved during the reach task on the stance leg.

Postural control describes the ability control body position in terms of balance and stability and body orientation in space. Palmieri et al. (2002) describe the purposes of evaluating postural control in clinical settings as: determining if a balance deficit exists, deciding if treatment is required, finding the most effective treatment and establishing the underlying cause of the balance deficit. Of the four clinical purposes of evaluating postural control, biomechanical analysis can help identify only if a deficit exists. The multi-systemic (neural, musculoskeletal, visual and vestibular) nature of the postural control system, makes it difficult to show a link between physiological changes and measures of postural control (Palmieri et al., 2002). Nevertheless, there is disagreement about which variable is most or least sensitive to changes in postural control (Palmieri et al., 2002).

Determining which measure of postural control to report is complicated by the number and inconsistencies of the variables reported. Centre of pressure (COP) measures are most often used to

quantify postural control. More than 50 COP variables have been recorded in the literature, comparing measures is difficult due to inconsistencies in naming, reporting and defining variables as well as in sampling frequencies and signal filters (Quijoux et al., 2021). Increases in the value of COP variables represents decreases in postural control. Studies often report several variables, which can complicate statistical analysis. Often, there is no justification for the choice of COP variable or clear description of what the variable is measuring (Palmieri et al., 2002; Quijoux et al., 2021).

For the purposes of this research, a single measure, COP total excursion (TE) (cm) was used to identify if there was a difference in postural control between GJH and non-GJH groups. COP signal was calculated from forces (F) (N) and moments (M) (N·m) measured by the inground force plate in the anterior-posterior (AP or y-axis) and medial-lateral (ML or x-axis) directions in Visual 3D software (C-Motion Inc, Kingston, ON, Canada) using the following equations:

$$\text{COP}_x = \frac{F_x d_z - M_x}{F_z} \quad \text{COP}_y = \frac{F_y d_z - M_y}{F_z}$$

Where force is applied on the top surface of the platform which has a height of zero in the motion capture volume (therefore COP in the superior-inferior (z) axis equals 0) and d indicates the distance between the electrical origin of the force plate and the centre of the surface of force plate (Robertson et al., 2014). TE (cm) was defined as the total length of the COP trajectory in both AP and ML directions and calculated using the following formula (Quijoux et al., 2021) where x represents the ML axis, y represents the AP axis and n represents the number of frames:

$$\text{COPTe (cm)} = \sum_n \sqrt{(x_{n+1} - x_n)^2 + (y_{n+1} - y_n)^2}$$

9.4.5 Gait

Participants performed barefoot overground gait on a 5m walkway in two conditions: (a) a self-selected speed and (b) at timed normalized (1.0 m/s) speed (Zeni & Higginson, 2009b). The timed condition was included to attenuate any confounding variables that may be attributed to gait speed (Zeni & Higginson, 2009a). A successful trial included full contact between the entire foot and the force plate. Five successful trials for each leg were collected for each participant (Laroche et al., 2011). Gait speed was recorded using a Browser timing system (Browser Timing Systems, Utah, USA). In the timed condition, participants were told to slow down or speed up their gait until they reached the normalized speed.

9.4.5.1 Dynamic Knee Joint Stiffness

DKS (Nm/kg/°) is the slope of the line when knee moment is plotted against the knee angle (Gustafson et al., 2016; Zeni & Higginson, 2009a, 2009a). Kinematic, kinetic and body segment inertial parameters were used in Newton-Euler inverse dynamics equations to calculate net knee joint moment during the weight-acceptance phase of gait (Robertson et al., 2014). DKS was calculated as the change in sagittal plane knee joint moment (M) divided by change in sagittal plane knee joint angle (θ):

$$\text{Dynamic knee stiffness (DKS)} = \frac{\Delta M}{\Delta \theta}$$

9.4.6 Diagnostic Criteria

9.4.6.1 The Beighton Score

The BS was conducted for all participants before testing based on recommendations for uniform testing in Juul-Kristensen et al. (2017) as recommended in the 2017 diagnostic criteria for hEDS and HSD (Juul-Kristensen et al., 2017; Malfait et al., 2017). The BS is a categorical scale where a clinician observes 5 joint positions and categorizes the range of motion achieved relative to standardized photos and descriptions of joint positions. The joint assessments are as follows: 1) passive apposition of the

thumb to the ventral and aspect of the forearm (shoulder flexed at 90°, elbow extended and hand pronated); 2) passive dorsiflexion of the fifth finger past 90° (elbow flexed at 90°, the forearm and hand pronated resting on a table); 3) hyperextension of the elbow beyond 10° (shoulder 90° abducted and hand supinated); 4) hyperextension of the knee beyond 10° in standing; and 5) forward flexion of the trunk, with knees straight, so the palms of the hands rest easily on the floor (Beighton et al., 1973; Juul-Kristensen et al., 2007) (Appendix B).

Juul-Kristensen et al. (2017) recommends specific test protocol script, which demonstrated substantial agreement for inter-reliability ($Kappa = 0.80$) and moderate agreement for in the fifth finger and elbow ($Kappa \geq 0.60$). Instead of the use of goniometer, photos from Beighton et al. (1973) and the descriptions of a positive or negative in the protocol script, and experimenter demonstration of the tested maneuvers determined the BS score (Juul-Kristensen et al., 2007, 2017). Warm muscles and stretching affect the BS. To attenuate the impact of intense physical activity or stretching before the testing protocol, participants spent 5-10 minutes resting between arriving to the lab and performing the BS (Castori et al., 2017; Juul-Kristensen et al., 2017). The full script and photos that was used for BS assessment are in Appendix B.

9.4.6.2 Disease Impact: Bristol Impact of Hypermobility Questionnaire (BIOH)

The BIOH is a condition-specific tool developed by clinicians and patients to help identify the impact of symptomatic GJH. It is a self-report tool with 55 items addressing symptoms (e.g., pain, fatigue, and joint instability) and impairments (e.g., activity limitations) (Palmer et al., 2020). Section A of the BIOH counts the number of 10 painful joint areas compared with the 5 joints assessed in the BS and, unlike the BS, assesses the impact of major and minor joints in all four limbs and the axial skeleton (Palmer et al., 2020). Palmer et al. (2020) showed strong known-group validity for BIOH which, in this case, means the ability to distinguish between sex and age matched groups with and without symptomatic GJH. The difference in total scores between groups is dramatic, more than three times the minimal detectable difference (the change that could be attributed to measurement error). All 55 questions on the

questionnaire were significantly different between groups but three individual items also showed known-group validity: number of painful joint areas, average pain and average fatigue. The BIoH also has excellent test-retest validity (ICC = 0.922) (Palmer et al., 2020).

The BIoH was constructed for symptomatic GJH but was adapted by Palmer et al. (2020) for a validity study which administered BIoH to a group diagnosed with symptomatic GJH and a version of the BIoH adapted for the general public to non-GJH (5PQ <2). Adaptations made the survey more relevant to those without symptomatic GJH and involved replacing “hypermobility” with “your general health” in 10 items of the 55-item questionnaire, changes which did not alter the validity of the questionnaire (Palmer et al., 2020).

This current study assumes, based on Palmer et al. (2020), that the BIoH for the general public has the same reliability and known-group validity as the BIoH. The BIoH version adapted for the general (non-symptomatic GJH) population was given to all participants (Appendix D). Participants were identified as symptomatic GJH or non-symptomatic GJH based on the interquartile ranges for total score (Table 4). (Palmer et al., 2020).

Table 2. Total score and three items from the BIoH that discriminate between symptomatic GJH and non-symptomatic GJH. Scores are given in median scores and interquartile ranges (IQR) in parentheses and taken from Palmer et al. (2020). Respondents were asked to consider the previous 7 days. *All differences are statistically significant and the median difference for total score exceeds the minimum detectable difference due to error (42 points) (Palmer et al., 2020).

Measure of BIoH	Maximum Score	Non-GJH	Symptomatic GJH	Difference in Median Score*
Total score (max 360)	360	81 (62.5-119)	231.5 (193-266.75)	150.5
Painful area count (Section A)	10	2 (1-3)	9 (7-10)	7
Average pain (Question 1)	10	1.5 (0.5-3)	6 (4-7)	4.5
Average fatigue (Question 5)	10	3 (1-5)	7 (5-8)	4

9.4.7 Descriptors

9.4.7.1 Limb Dominance Testing

There is some evidence that GJH is more common on the non-dominant side (Verhoeven et al., 1999) but there is difference in performance on the mSEBT based on leg dominance (Picot et al., 2021). The task of kicking a ball has been shown to significantly correlate with footedness preference and substantial test-test reliability (Kappa = 0.77) (Schneiders et al., 2010). To determine footedness, participants were asked to kick a ball. The foot used to kick a ball was identified as the dominant lower limb.

9.4.7.2 Pain

The Numeric Pain Rating Scale (NPRS). The Numeric Pain Rating Scale (NPRS) was used to assess pain during reaching tasks. The NPRS is an 11-point scale from 0 (no pain at all) to 10 (worst pain imaginable) (Appendix F). No pain scales have been validated on GJH populations, but the NPRS produces valid data on OA-related knee pain and has high test-retest reliability (ICC = 0.95) (Alghadir et al., 2018).

9.4.7.3 Physical Activity

International Physical Activity Questionnaire (IPAQ). Physical activity was measured using the long version of the International Physical Activity Questionnaire (IPAQ) which collects self-reported types and level of health-related physical activity in the previous 7 days (Appendix E). Scores can be calculated for total physical activity, walking, and moderate- and vigorous-intensity activities. When scored as continuous variable (MET-min/week) scores are divided into 3 levels of physical activity: (a) high (at least 3000 total MET-min/week or 1500 vigorous MET-min/week), (b) moderate (600 – 3000 total MET-min/week) or (c) low (less than 600 total MET-min/week). The IPAQ has acceptable test-retest reliability and criterion validity, at the same level of other established self-reports in 18-65 year-

olds in diverse settings (Craig et al., 2003). Although no covariates have been identified for GJH, type, volume and intensity of physical activity may factor into GJH symptoms (Castori et al., 2017).

10 Statistical Analyses

Statistical analyses were conducted in RStudio (RStudio: Integrated Development for R. RStudio, PBC, Boston, MA). Descriptive statistics (means, medians, standard deviations, and ranges) were conducted separately for foam, no-foam and timed no-foam conditions and gait for variables of interest (Table 6). Data was tested for normality using the Shapiro-Wilk test. For ANOVA, Levene’s test determined if data violated the assumption of homogeneity of variance.

To address the primary research objective, three, two-tailed, two-way mixed measures analysis of variances (ANOVA) were conducted for the mSEBT, to model the main effects of group (GJH and non-GJH) and condition (foam, no-foam and timed no-foam) and the interaction of group and condition on composite MRD, composite MKA and composite COPTE (Table 6). For DKS during gait, a Mann Whitney U test was performed to compare dynamic gait in the timed condition between and groups (GJH and non-GJH). Significance for all statistical tests was set at $p < 0.05$ ($\alpha=0.05$).

Table 3. Factors, levels and variables of interest for a 2X3 (group X condition) mixed measures ANOVA statistical test to address the primary research objective that compared performance between GJH and non-GJH in kinematic and kinetic variables in the mSEBT balance task.

Factors	Levels	Dependent Variables*
Group (Between-subjects)	GJH	MRD _{comp} COPTE _{comp} MKA _{comp}
	Non-GJH	
Condition (Within-subjects)	Foam	
	No foam	
	Timed (no foam)	

Abbreviations: MRD_{comp} = maximum reach distance, composite score; COPTE_{comp} = centre of pressure total excursion, composite score; MKA_{comp} = maximum knee flexion angle, composite score.

Since no significance was found for main effects, there was no need to adjust for family wise error. However, to fully address the primary hypothesis, multiple pairwise comparisons were analyzed to investigate if there was difference between conditions. Family-wise error was addressed using the Holm-Bonferroni Method. The following formula was used to find the adjusted significance level for the 9 pairwise comparisons (three conditions for MRD_{comp}, COPTE_{comp} and MKA_{comp}, respectively):

$$\alpha' = \frac{\text{Target Alpha Level } (\alpha = 0.05)}{n - \text{rank number of pair} + 1}$$

Where n is number of statistical tests (three per dependent variable) and rank number of pair was determined by the degree of significance of p-values from each statistical test. After the Holm-Bonferroni adjustment significant level was determined to be $\alpha' = 0.0008$. There was no significant difference between conditions for any of the dependent variables.

To address the secondary research objective, two hierarchical multiple regressions were used to determine if there is an association between (i) BS and MRD_{comp}, (ii) BIoH and MRD_{comp}. In both models, MRD_{comp} was the dependent variable and physical activity (IPAQ) was entered first as the covariate.

11 Results

Of the 28 participants included in this analysis, two were male and 26 were female with a mean age of 24.6 ± 4.1 years (Table 5, 6). No differences were observed between GJH and non-GJH groups in disease impact as indicated by the BIoH (107.5 ± 48.2 versus 78.4 ± 26.8 respectively, $p = 0.06$), physical activity as recorded on the IPAQ (4545.9 ± 4034.7 MET-min/week versus 5447.5 ± 3506.8 MET-min/week respectively, $p = 0.5$), self-selected gait speed collected in the lab (1.2 ± 0.07 m/s versus 1.2 ± 0.1 m/s respectively, $p = 0.9$), BMI (24.1 ± 5.0 kg/m² versus 23.5 ± 3.8 kg/m² respectively, $p = 0.7$) or the difference in knee pain before and after the dynamic balance task (0.3 ± 0.7 versus 0.1 ± 0.3 respectively, $p = 0.3$). Due to equipment failure, all gait trials for one participant in the GJH group were erroneous and not included in the analyses. As well, COPTE for one condition for two participants in the non-GJH group (one no foam condition and one timed condition) were deemed erroneous due to noise larger than expected and not included in the analyses.

Table 4. Count and proportion of self-reported participant race.

Race	Total (n = 28)		Non-GJH (n=14)		GJH (n = 14)	
	Count	Proportion (%)	Count	Proportion (%)	Count	Proportion (%)
White	15	53.6	8	57.1	7	50.0
South Asian	5	17.9	3	21.4	2	21.4
East Asian	5	17.9	1	7.1	4	28.6
Middle Eastern	1	3.6	1	7.1	0	0.0
Latine/Latinx, White	1	3.6	0	0.0	1	7.1
Middle Eastern, White	1	3.6	1	7.1	0	0.0

Table 5. Means, standard deviations, minimum and maximum values for descriptors. NPRS values represent the difference in knee pain (average of the dominant and non-dominant knee) between the start and end of the Modified Star Excursion Balance Test.

	Total (n = 28)				Non-GJH (n=14)				GJH (n = 14)			
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Age (years)	24.6	4.1	18.0	34.0	24.7	4.2	19.0	31.0	24.6	4.2	18.0	34.0
BMI (kg/m ²)	23.8	4.4	16.9	36.7	23.5	3.8	16.9	29.3	24.1	5.0	18.9	36.7
BS (/9)	3.6	3.0	0.0	9.0	1.0	1.3	0.0	4.0	6.2	1.3	5.0	9.0
BloH (/38-360)	93.0	41.0	40.0	239.0	78.4	26.8	40.0	116.0	107.5	48.2	59.0	239.0
IPAQ (METmin/week)	4996.7	3737.6	770.0	15039.0	5447.5	3506.8	786.5	12321.0	4545.9	4034.7	770.0	15039.0
Gait speed (m/s)	1.2	0.1	1.0	1.4	1.2	0.1	1.0	1.4	1.2	0.07	1.1	1.3
NPRS (/11)	0.2	0.5	0.0	2.5	0.1	0.3	0.0	1.0	0.3	0.7	0.0	2.5

Abbreviations: SD = Standard Deviation, Min = Minimum Value, Max = Maximum value, BMI = Body Mass Index, BloH = Bristol Impact of Hypermobility Questionnaire, IPAQ = International Physical Activity Questionnaire, NPRS = Numeric Pain Rating Scale.

$$\text{MRD}_{\text{reachdirection}} (\%) = \frac{\text{mean of 3 trials in the reach direction (cm)}}{\text{standing limb length (cm)}} \times 100$$

Second, a normalized composite score (MRD_{comp}) was generated as the average of all the normalized MRDs for all three directions (anterior (ANT), posterolateral (PL), posteromedial (PM)) for each participant in each condition using the following equation (Picot et al., 2021):

$$\text{MRD}_{\text{COMP}} (\%) = \frac{\text{MRD}_{\text{ANT}}(\%) + \text{MRD}_{\text{PL}}(\%) + \text{MRD}_{\text{PM}}(\%)}{3}$$

Composite scores of maximum knee joint angle (MKA_{COMP}) and COP total excursion ($\text{COPT}_{\text{COMP}}$) were also calculated as the combined averages of maximum knee joint angle and COP total excursion, respectively, for each reach in all three directions.

The beginning of a reach attempt was defined as a movement of greater than 1cm of the reaching leg from the start position. The end of a reach attempt was defined as the return to within 1cm of the starting position. Movement of the reaching leg was calculated between the laboratory origin and the medial malleolus of the reaching leg. In cases where participants did not start and end in the same position, the beginning and end of reach attempts were identified visually in Visual3D.

Net joint moments (Nm) were normalized by body weight (kg) (Davis & DeLuca, 1996; Moio et al., 2003). DKS was determined during gait by (1) identifying the period between peak knee extension and peak knee flexion of the weight-acceptance phase of gait (approximately 0-12% of the gait cycle); (2) plotting net knee joint moment (y-axis) and knee angle (x-axis); (3) fitting a linear regression curve to the data points; (4) calculating DKS as the slope of the fitted curves (Davis & DeLuca, 1996; Gustafson et al., 2016). The non-dominant leg was used for analysis of DKS because in those with GJH it is the more hypermobile knee (Beckley et al., 2022; Simmonds, 2022).

No significant main effect was found between MRD_{comp} and group ($F_{(1,26)} = 1.34$; $p = 0.26$) (Figure 5; Table 8), showing there was no difference between GJH and non-GJH groups in MRD_{comp} .

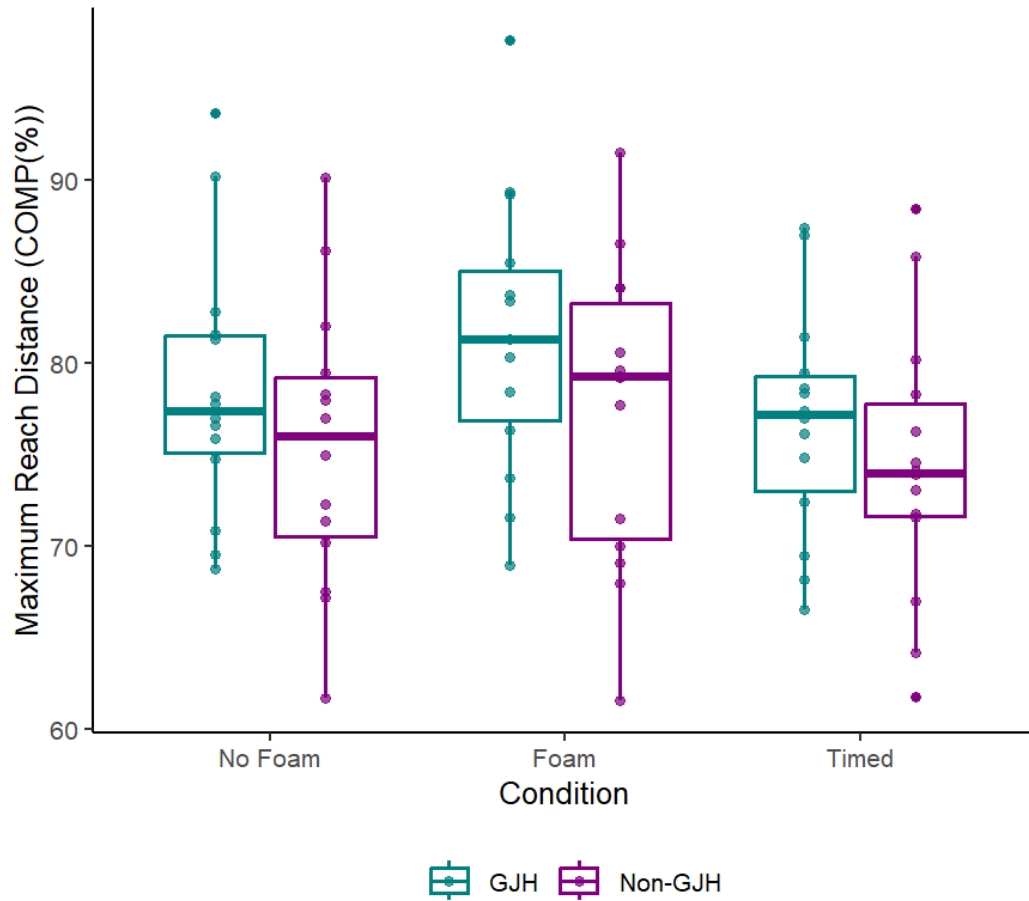


Figure 5. Boxplot of primary dependent variable (Maximum Reach Distance, composite score) (%) for the group with Generalized Joint Hypermobility (GJH) and the age- and sex-matched comparison group (non-GJH) in all conditions of the Modified Star Excursion Balance Test.

11.2 Centre of Pressure Total Excursion

No significant main effect was found between $\text{COPTe}_{\text{comp}}$ and group ($F_{(1,26)} = 0.0000003$; $p = 0.99$) (Figure 6; Table 8), showing there was no difference between GJH and non-GJH groups in $\text{COPTe}_{\text{comp}}$.

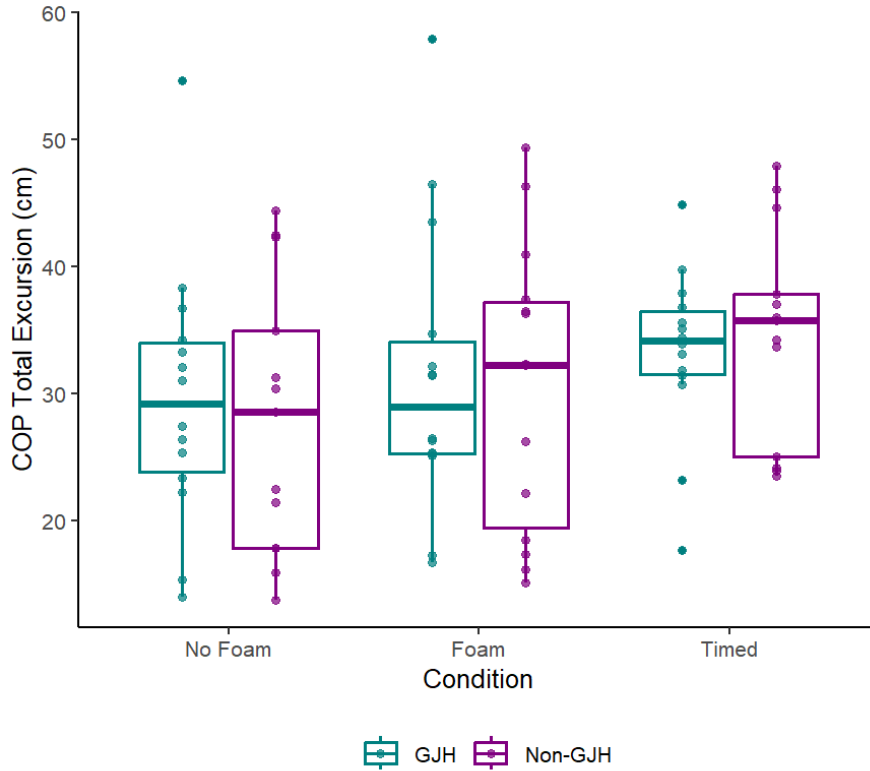


Figure 6. Boxplot of Centre of Pressure Total Excursion (composite score) (cm) of the group with Generalized Joint Hypermobility (GJH) and the age- and sex-matched comparison group (non-GJH) in all conditions of the Modified Star Excursion Balance Test.

11.3 Maximum Knee Angle

No significant main effect was found in MKA_{comp} between groups ($F_{(1,26)} = 0.60$; $p = 0.45$)

(Figure 7; Table 8), showing there was no difference between the amount of maximum knee flexion angle between non-GJH and GJH groups during the mSEBT.

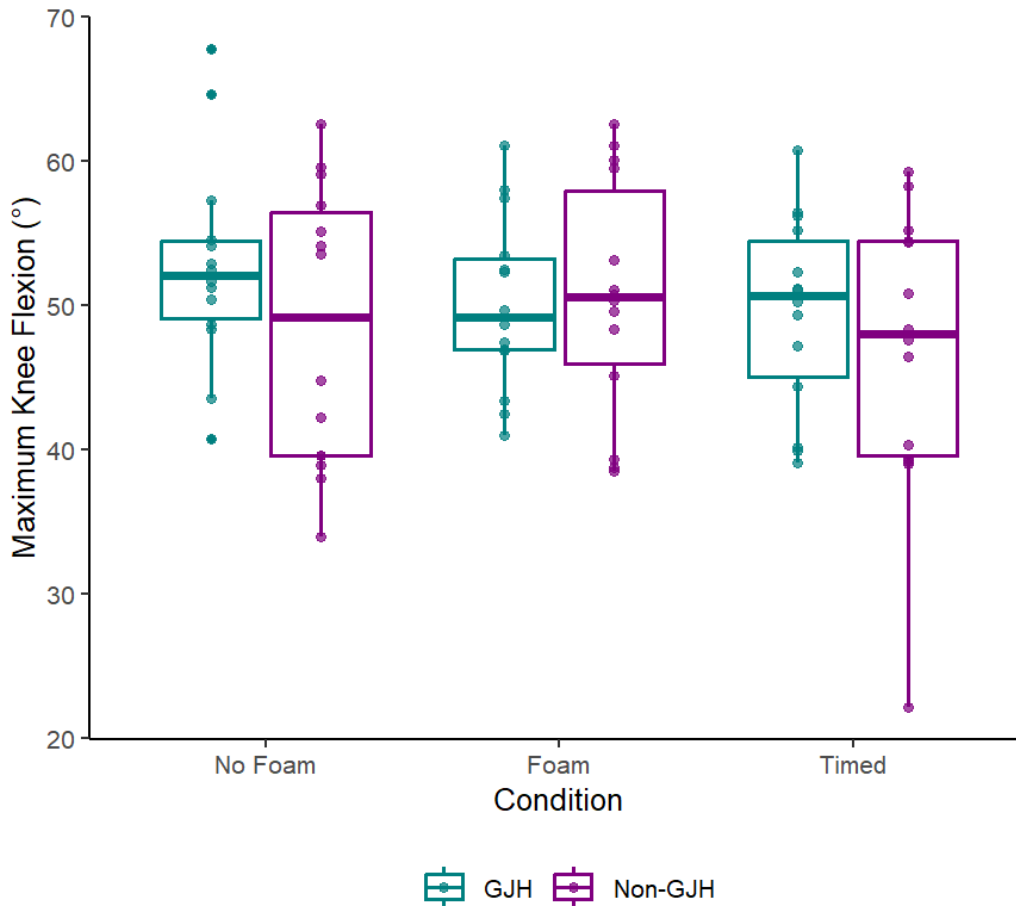


Figure 7. Boxplot of Maximum Knee Angle (composite score) (°) of the group with Generalized Joint Hypermobility (GJH) and the age- and sex-matched comparison group (non-GJH) in all conditions of the Modified Star Excursion Balance Test.

11.4 Dynamic Knee Stiffness

No significant difference was found between GJH and non-GJH groups for DKS in the timed condition (0.05 ± 0.02 vs. 0.06 ± 0.03 ; $W_{(1,26)}= 65$; $p = 0.22$) (Figure 8,9; Table 8).

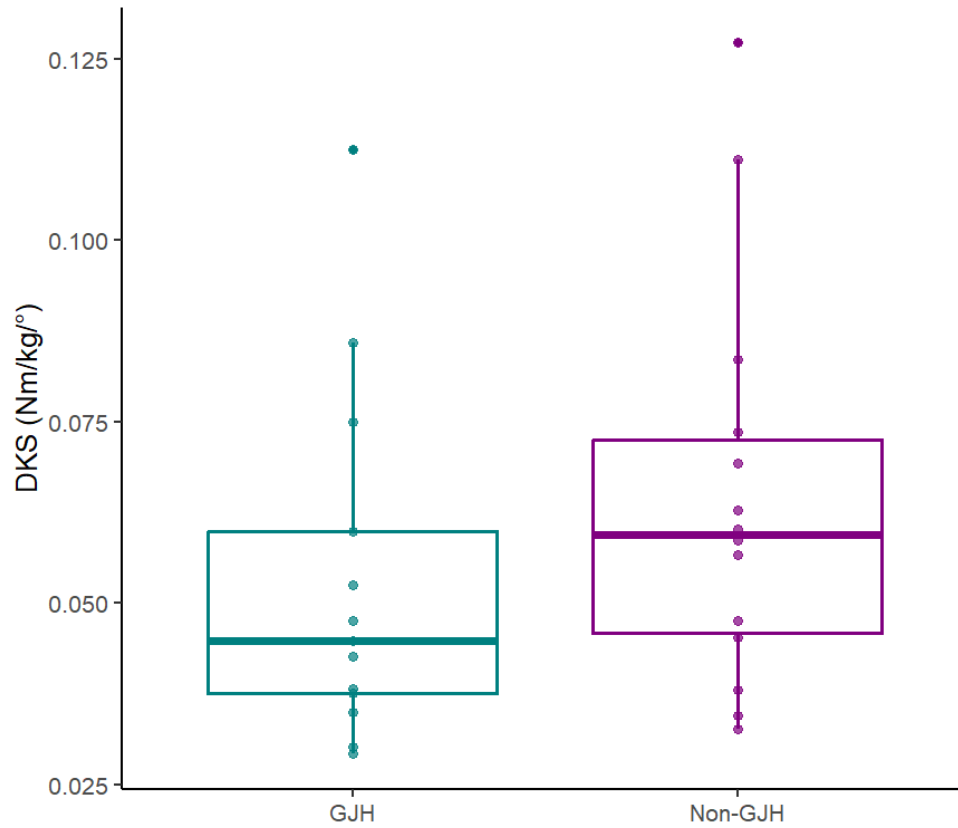


Figure 8. Boxplot of Dynamic Knee Stiffness (DKS) (Nm/kg/°) for the non-dominant leg in the timed gait condition comparing the group with Generalized Joint Hypermobility (GJH) (n = 13) and the age- and sex-matched comparison group (non-GJH) (n = 14).

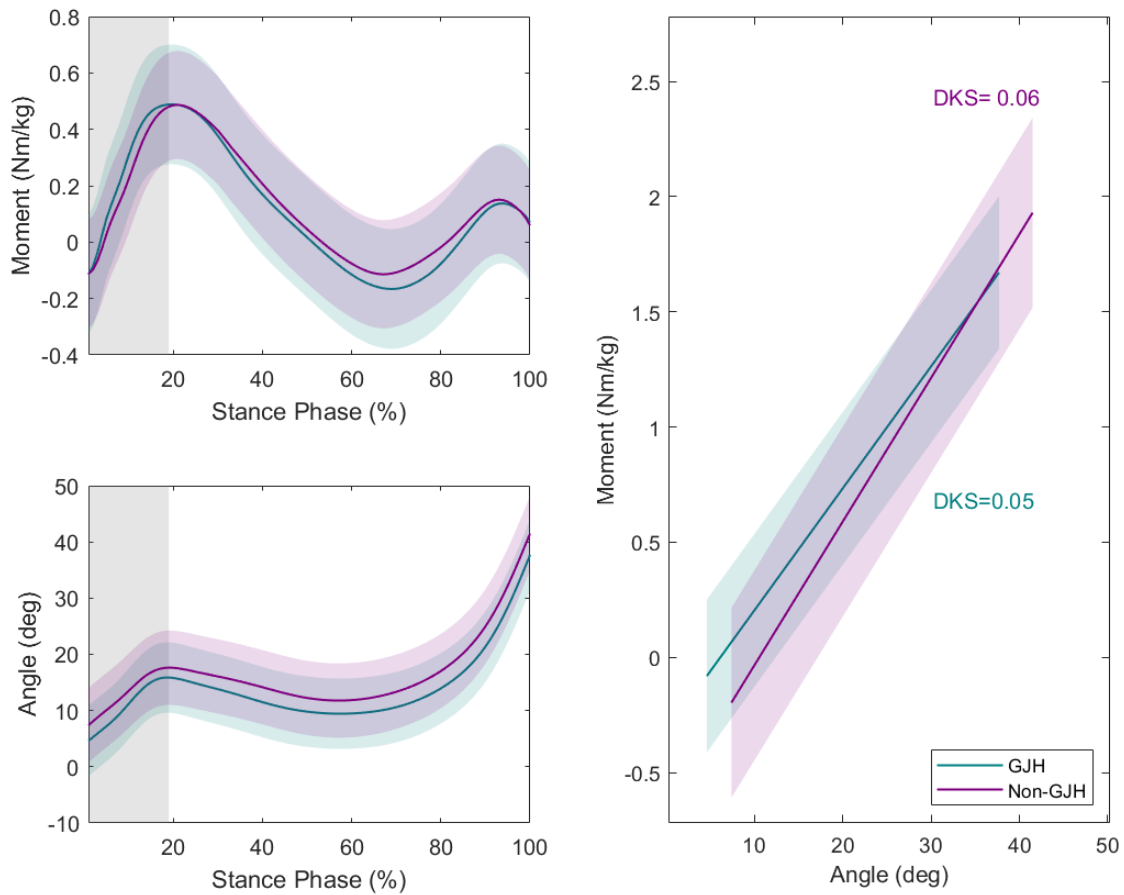


Figure 9. Ensemble averages of normalized moments (top left), knee angle (bottom left) ($^{\circ}$) and Dynamic Knee Stiffness (DKS) (right) (Nm/kg°) in the non-dominant leg in Generalized Joint Hypermobility (GJH) and non-GJH groups. Moments and angles represent the weight acceptance phase of gait. The shaded area shows the average linear region (from minimum knee moment to maximum knee flexion angle) used for calculating DKS.

11.5 Beighton Score versus Disease Impact

The regression models identified that the BS ($R^2 = 0.07$, $\beta = 0.07$, $F_{(2,,26)} = 0.10$, $p = 0.90$) (Figure 10; Table 6) and the BIoH ($R^2 = 0.08$, $\beta = 0.02$, $F_{(2,,26)} = 0.05$, $p = 0.95$) (Figure 10; Table 6) were not significantly associated with MRD_{comp} . In terms of disease impact, results of the BIoH showed that, from the entire sample, one participant met the criteria for symptomatic GJH (Figure 11).

Results from the IPAQ showed eight participants (three GJH and five non-GJH) with outlier values (Figure 12). Scoring and data processing guidelines for the IPAQ define outliers as total scores greater

than 960 MET-min/day (6720 MET-min/week) or 16 hours per day with the assumption that the average person sleeps 8 hours per day (*Guidelines for the Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ). Short and Long Forms, November 2005.*). Outlier values were included in the analysis because these data points and overall averages fell within published values of other university graduate and undergraduate students (Gaweł-Dąbrowska et al., 2016; Maddison et al., 2007).

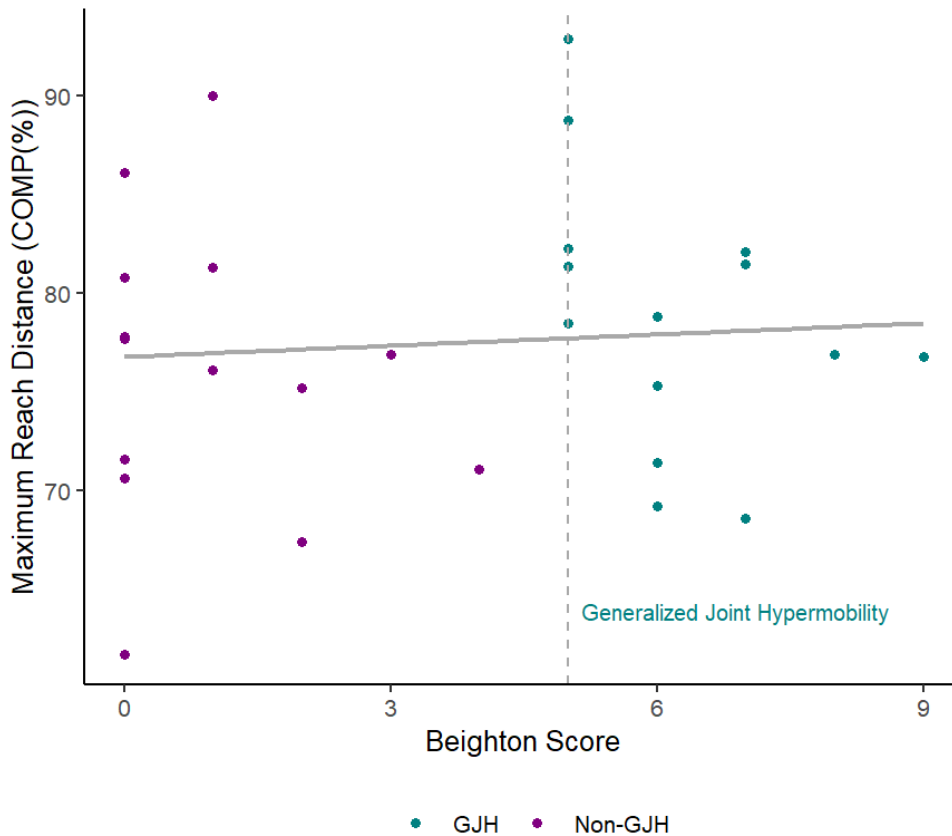


Figure 10. Visualization of the regression analysis to determine the association between the current diagnostic criteria (Beighton Score) for generalized joint hypermobility and performance on dynamic balance tasks (MRD_{comp}). Dashed line indicates the Beighton Score (5) cutoff for generalized joint hypermobility. The solid grey line is the regression line ($R^2 = 0.07$, $\beta = 0.07$, $F_{(2,,26)} = 0.10$, $p = 0.90$). Dotted line indicates cut off for Generalized Joint Hypermobility (Beighton Score ≥ 5).

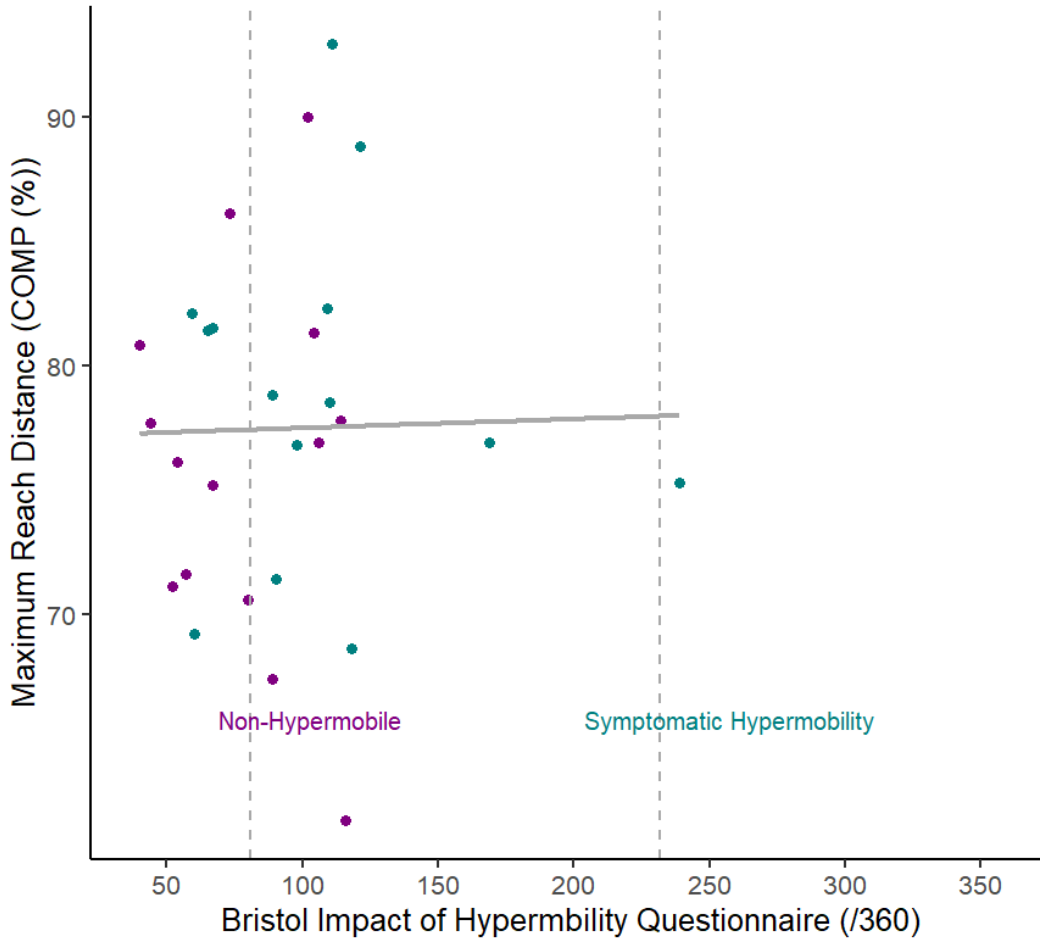


Figure 11. Visualization of the regression analysis to determine the association between the measure of disease impact (Bristol Impact of Hypermobility Questionnaire) for generalized joint hypermobility and performance on dynamic balance tasks (MRD_{comp}). Dashed lines indicate published median scores for those without hypermobility and those with symptomatic hypermobility. The solid grey line is the regression line ($R^2 = 0.08$, $\beta = 0.02$, $F_{(2,26)} = 0.05$, $p = 0.95$). Dotted lines indicate median scores for non-hypermobility and symptomatic hypermobile groups based on Palmer and colleagues (2020).

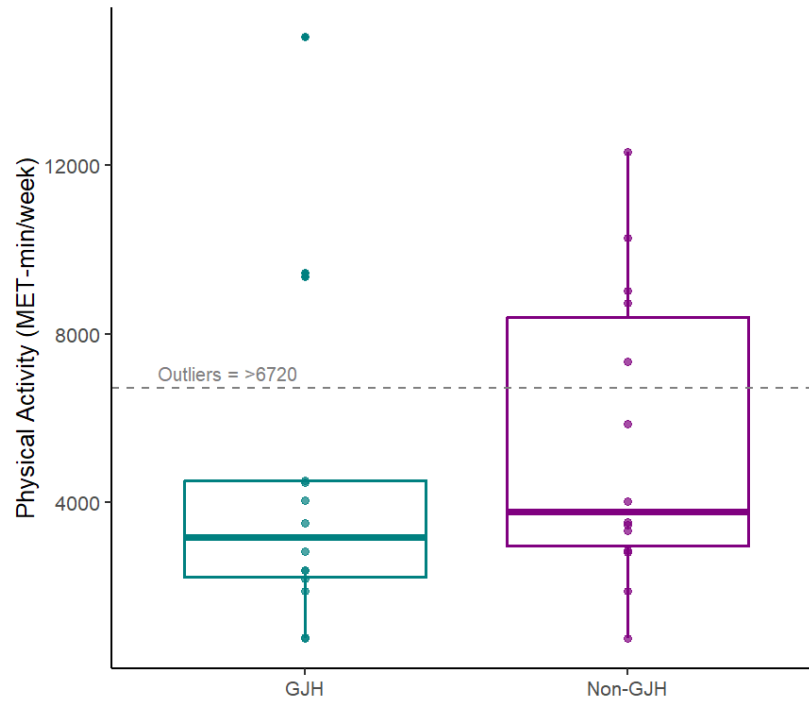


Figure 12. Boxplot showing results of International Physical Activity Questionnaire (IPAQ). Outliers are defined by IPAQ scoring guidelines as 6720 MET-min/week.

Table 6. Means, standard deviations, minimum and maximum values for dependent variables by leg, and t-values or W-scores and p-values for independent t-tests between dominant and non-dominant legs for each dependent variable. Mann Whitney U test was used for dynamic knee stiffness values, which had a non-normal distribution.

	Total (n = 28)				Non-Dominant (n = 28)				Dominant (n = 28)				t-Test	
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	t-value	p-value
MRD_{COMP} (%)	77.1	7.8	59.3	95	77.8	7.7	61.6	95	76.4	8.0	59.3	90.8	-0.67	0.50
COPT_E_{COMP} (cm)	31.2	8.6	15.0	54.2	30.5	7.47	15.9	42.1	31.8	9.7	17.8	54.2	0.55	0.58
MKA_{COMP} (°)	49.4	7.9	29.4	63.7	49.7	7.0	37.5	59.6	49.2	8.7	29.4	63.7	-0.23	0.82
DKS (Nm/kg/°)	0.06	0.03	0.03	0.13	0.06	0.02	0.03	0.13	0.06	0.2	0.4	0.11	*W = 424	0.31

*Indicates use of Mann Whitney U test in the case of non-normal distribution. Abbreviations: SD = Standard Deviation, Min = Minimum Value, Max = Maximum value, COPT_E_{comp} = Centre of Pressure Total Excursion (composite score), MKA_{comp} = Maximum Knee Flexion Angle (composite score), MRD_{comp} = Maximum Reach Distance, DKS = Dynamic Knee Stiffness (timed condition, non-dominant leg). All are reported as composite scores.

Table 7. Means, standard deviations, minimum and maximum values for dependent variables in each condition in the Modified Star Excursion Balance Test (mSEBT) and during timed and untimed gait.

	Condition	Total (n = 28)				Non-GJH (n=14)				GJH (n = 14)			
		Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
MRD_{COMP} (%)	All	77.3	7.6	61.6	97.6	75.7	7.7	61.6	91.5	78.9	7.1	66.6	97.6
	No Foam	77.0	7.5	61.7	93.6	75.4	7.7	61.7	90.1	78.5	7.1	68.8	93.6
	Foam	79.4	8.1	61.6	96.6	77.3	8.3	61.6	91.5	81.5	7.6	69	97.6
	Timed	75.5	6.8	61.8	88.4	74.4	7.4	61.8	88.4	76.7	6.2	66.6	87.4
COPT_E_{COMP} (cm)	All	31.3	9.9	13.8	57.9	31.0	10.4	13.8	49.3	31.5	9.5	14.0	57.9
	No Foam	28.8	10.3	13.8	54.7	28.0	10.7	13.8	44.4	29.6	10.3	14.0	54.7
	Foam	31.0	11.1	15.2	57.9	30.5	11.4	15.2	49.3	31.5	11.3	16.7	57.9

	Timed	33.9	7.5	17.7	48.0	34.6	8.5	23.5	48.0	33.3	6.7	17.7	44.8
MKA_{COMP} (°)	All	49.7	8.1	22.1	67.8	48.6	9.3	22.1	62.6	50.8	6.6	39.0	67.8
	No Foam	50.5	8.8	34.0	67.8	48.4	9.7	34.0	62.5	52.7	7.2	22.1	67.8
	Foam	50.6	7.1	38.5	62.6	46.8	10.1	22.1	59.3	50.1	6.0	41.0	61.1
	Timed	47.8	8.5	22.1	60.8	75.3	7.4	64.2	88.4	49.5	6.7	39.0	60.8
DKS	Timed (Nm/kg/°)	0.06	0.03	0.03	0.13	0.06	0.03	0.03	0.13	0.05	0.03	0.03	0.11
	Timed (Nm/°)	3.8	1.5	1.8	7.1	4.1	1.5	1.8	7.1	3.5	1.5	2.0	7.1
	Self-selected (Nm/kg/°)	0.07	0.03	0.02	0.13	0.07	0.03	0.03	0.13	0.07	0.03	0.03	0.15
	Self-selected (Nm/°)	4.6	2.0	1.5	9.4	4.56	1.9	1.5	7.7	4.6	2.1	1.7	9.5

All measures of dynamic balance are as composite scores. Abbreviations: SD = Standard Deviation, Min = Minimum Value, Max = Maximum value, COPTE = Centre of Pressure Total Excursion, MKA = Maximum Knee Flexion Angle, MRD = Maximum Reach Distance, DKS = Dynamic Knee Stiffness. Gait conditions for DKS were self-selected gait speed and timed (gait speed normalized to 1 m/s).

12 Discussion

The three objectives of this project were to (1) determine if the mSEBT, a clinically accessible test of dynamic balance, could be used to identify the presence of GJH, (2) characterize dynamic knee stiffness of those with and without GJH using dynamic knee stiffness, and (3) determine the associations of performance on the mSEBT to the diagnostic criteria (BS) and a validated measure of disease impact (BIOH). No difference was found between GJH and non-GJH groups in the measurements of the mSEBT (MRD_{comp} , $COPT_{comp}$, MKA_{comp}) or DKS observed during gait. The lack of difference observed likely reflects that this sample included only one participant who experienced symptomatic GJH. The remaining sample demonstrated signs of GJH but did not experience symptoms, perhaps suggesting absence of symptoms, milder or early-stage disease. There was no association between disease impact or number of hypermobile joints in this largely asymptomatic population and performance on the mSEBT. The results of this study suggest that the mSEBT and DKS are not appropriate measures to differentiate between asymptomatic GJH and non-GJH groups in non-athlete university graduate and undergraduate students.

12.1 Symptomatic Generalized Joint Hypermobility

The results of this study indicate that biomechanics of dynamic balance tasks may not be distinct in those with asymptomatic GJH from their age-matched healthy peers. This finding contrasts with some published work. In previous studies comparing non-GJH with asymptomatic and symptomatic GJH in stair-climbing, greater biomechanical differences were seen between healthy and symptomatic GJH compared with healthy and asymptomatic GJH (Bates et al., 2021b; Luder et al., 2015). Luder and colleagues (2015) compared females without GJH ($n = 67$; aged 24.8 ± 5.4) and those with GJH ($n = 128$; aged 25.8 ± 5.4). The hypermobile group had three subgroups: symptomatic ($n = 56$; aged 25.3 ± 5.4), asymptomatic ($n = 47$; aged 25.7 ± 5.3) and “without subclassification,” meaning those whose symptom profile was not reported ($n = 25$; aged 27.1 ± 5.8) (Luder et al., 2015). The results showed lower muscle activation in the quadriceps during stair ascent in asymptomatic and symptomatic GJH (93.9 ± 39.2 %MVC) compared with non-GJH (110.2 ± 43.9 %MVC). In the GJH groups, those with symptomatic

GJH had lower muscle activation (88.4 ± 32.5 %MVC) than those with asymptomatic GJH (98.2 ± 47.1 %MVC). The authors suggested that clearer differences in muscle activation patterns may require more challenging activities and/or fatigue-inducing movements (Luder et al., 2015). Bates and colleagues (2021b) compared those without GJH ($n = 22$; aged 33 ± 9 ; 20 females), with asymptomatic GJH ($n = 23$; 28 ± 6 , 19 females) and symptomatic GJH ($n = 21$; aged 28 ± 5 ; 15 females) in stair climbing. Statistical parametric mapping showed differences between groups that the authors suggested may represent a spectrum of kinematic and kinetic characteristics from non-GJH to symptomatic GJH with asymptomatic GJH in between (Bates et al., 2021b). During stair descent, those with symptomatic GJH had greater hip flexion than the other groups. During stair ascent, those with symptomatic GJH spent more time in stance phase, and had lower ankle plantarflexor moment and smaller knee extension moment than those in the non-GJH and asymptomatic GJH groups (Bates et al., 2021b). In terms of joint power, those with symptomatic GJH had less power at the ankle than those with asymptomatic GJH and more power at the knee than those without GJH. Additionally, those with symptomatic GJH had smaller knee extension moments than those without symptoms (Bates et al., 2021b). While not measured in this study, it is possible that small differences exist between GJH and non-GJH in knee and ankle power and angles during the mSEBT. Taken together, this group of studies suggests that there appears to be little or no difference between asymptomatic GJH and non-GJH groups in biomechanical features during performance of a variety of tasks, including the mSEBT; however, there may be a difference between symptomatic GJH and non-GJH.

Dynamic knee stiffness did not differ between those with and without GJH in the current study. These findings support the 2015 meta-analysis of gait kinematics and kinetics, which analyzed five papers each with sample sizes from 12-19 participants. The meta-analysis found no evidence that gait variables (that did not include DKS) differ between GJH and non-GJH groups (Bates & Alexander, 2015). The lack of difference in DKS may reflect the lack of symptomatic participants in the sample. Measuring DKS on a group of people with symptomatic GJH and comparing it to non-GJH and asymptomatic GJH groups may

provide more information (Luder et al., 2015). It may also be that differences exist in dynamic joint stiffness at the ankle and not the knee. Rigoldi and colleagues (2012) found that those with symptomatic GJH have lower ankle stiffness than healthy controls (0.056 ± 0.03 vs. 0.083 ± 0.03). Overall, the biomechanical measures selected in this study cannot be used to distinguish between those with asymptomatic GJH and those without GJH.

12.1.2 Pain

The lack of participant self-reported knee pain reported before and after the mSEBT is likely critically important to the negative findings observed in this study. Chronic and acute musculoskeletal pain in multiple joints is a key symptom of symptomatic GJH (Castori et al., 2017; Chopra et al., 2017). Joint pain alters biomechanics. Experimentally-induced knee pain in healthy participants ($n = 34$; aged 25.6 ± 5.5) resulted in reduced knee joint moments similar to those seen with moderate knee OA (Henriksen et al., 2010). Exercise-induced joint pain also alters biomechanics. Boyer and Hafer (2019) compared gait in healthy controls and those with knee OA before and after a bout of exercise (20-minute walk test). Kinetics of those with OA that experienced a flare of knee pain after exercise ($n = 8$; aged 62.1 ± 1.9 years) differed from those with OA who did not have a pain flare ($n = 11$; aged 62.6 ± 1.9 years) and healthy controls ($n = 17$; aged 64.5 ± 1.5 years). When comparing those with OA with and without a pain flare the pain flare resulted in decreased knee flexion moment ($d = 0.66$), first and second knee adduction moment ($d = 0.49$), knee internal rotation moment ($d = 0.82$) and ankle eversion ($d = 0.73$) (Boyer & Hafer, 2019). Similarly, when comparing females with and without patellofemoral pain syndrome (PFPS), those with PFPS ($n = 40$; aged 15-28 years) had lower knee extensor strength and reduced single leg vertical jumping ability on the most symptomatic knee compared to health controls ($n = 20$; aged 17-28 years) (Thomeé et al., 1995). These studies indicate that it is pain, perhaps not necessarily the underlying condition of OA or PFPS, that altered biomechanics. From this perspective, the lack of pain, reported before and after the mSEBT, rather than the presence or absence of GJH in this study, may help explain the lack of biomechanical difference observed between groups.

12.1.3 Disease Impact

The results of this study do not resolve if disease impact, rather than number of hypermobile joints, may affect dynamic balance performance because the participants with GJH in this study, for the most part, did not experience symptoms. In university students, neither disease impact measured by the BIoH nor GJH measured by the BS, are associated with performance on the mSEBT. The BIoH reflects symptoms (e.g., pain, fatigue, and joint instability) and impairments (e.g., activity limitations) (Palmer et al., 2020). To determine if there is an association between disease impact and biomechanics, participants with symptomatic GJH are required. Accomplishing this could entail recruiting participants based on a cluster of common symptomatic GJH-specific symptoms, such as 5-10 joint painful joint areas, recurrent multiple joint subluxations or dislocations and chronic fatigue (Palmer et al., 2020). By recruiting participants based on symptoms rather than BS, a higher proportion of those with symptomatic GJH, even those not yet diagnosed, could be included in future studies.

12.2 Measurement Principles

Of the measures used in this study, there were variances around the mean that were larger than the difference between groups (Table 8). This relatively larger “noise” to signal of interest ratio diminished the ability of these measures to find a statistical difference between groups. Using statistical analysis to determine the difference between groups relies in part on groups means and pooled variance. Take, for example, the impact of variance larger than the difference of means on effect size. When using Cohen’s *d* as a measure of effect size, it is defined as the magnitude of the difference between two means using this equation (Kelley & Preacher, 2012):

$$\text{Effect Size (d)} = \frac{\text{mean}_a - \text{mean}_b}{\text{pooled variance}}$$

The larger the pooled variance in relation to the difference between the means, the lower the effect size. This points to the importance of using a measure-specific effect size for the measure and the population of interest in sample size calculation, when possible. Since MRD_{comp} is a novel measure for those with GJH, effect size for kinematics and kinetics in the population of interest were used. Future study designs may

consider effect sizes for the GJH population (asymptomatic or symptomatic) and for the measure of interest as well as measures that have expected variance smaller than the difference between groups means.

Normal distributions are also important for robust statistical analysis. The lack of variability in DKS between all participants resulted in data that were not normally distributed (Figure 12). Increasing the sample size for DKS or choosing a measure that produces greater between-person variability, may have resulted in more normally distributed data for the groups in this study. Nonetheless, dynamic joint stiffness may be appropriate measurement for a group with symptomatic GJH, as demonstrated by Rigoldi et al. (2012). As the results of this study demonstrate, a measure with greater variability between participants and groups may be necessary for comparing asymptomatic GJH and non-GJH groups.

12.3 Conditions

Unlike previous studies, measures used in the current study were not sensitive enough to detect a difference between conditions. Previous findings showed that performance on the mSEBT diminished with increased cognitive demand when participants listened to music or used a smartphone (Hyong, 2015). When compared to the cognitive demands of smartphone usage, it may be that the cognitive demands of the timed condition in this study may not have been sufficient to alter performance on the mSEBT. In previous studies using unstable conditions, the mSEBT foam condition elicited the expected changes in performance between groups (Nozu et al., 2021; Sabin et al., 2010). Nozu et al. (2021) compared 20 healthy participants aged 23.9 ± 3.0 years in the posteromedial direction in timed foam and timed no foam conditions. In the timed foam condition, participants demonstrated shorter MRD, greater flexion at the hip and knee and more and anterior center of mass and COP (Nozu et al., 2021). Sabin et al. (2010) compared collegiate basketball players ($n = 16$) to non-athletes ($n = 16$) aged 19 to 22 in posterior, medial and lateral directions in foam and no foam conditions. The non-athletes reached further in all directions and the composite score. Additionally, MRD composite score in the medial and posterior directions were lower in the foam condition (Sabin et al., 2010).

During the mSEBT in the current study, altering the conditions by changing surface (no foam, foam) or adding a time requirement, did not affect performance, knee angle or COPTe. It is interesting to note that MKA was not sensitive to different conditions of mSEBT. Since Nozu et al (2021) had participants move at 60 BPM for both foam and no foam condition, it is possible that the additional cognitive challenge of timed movement on the foam may have elicited a difference not observed in the current study.

12.4 Factors Affecting Performance During Dynamic Balance

Findings from the current study examining dynamic balance in those with GJH for the first time may have revealed some confounding variables. Although confounding variables have been identified for the mSEBT and for those with GJH, not all factors affecting performance in the population could be predicted before this first effort to use biomechanics of dynamic balance to differentiate GJH from healthy peers. Differences in type of physical activity among non-athletes, the measure of physical activity and age may have affected the results of the mSEBT.

12.4.1 Type of Physical Activity

Type of current or previous physical activity and exercise may have influenced performance on the mSEBT in the current sample. Through screening during the recruitment process, the sample for the current study self-reported participating in fewer than 4X30 minutes of structured exercise per week (Bressel et al., 2007; Sabin et al., 2010), or regular single leg balance training, for the 8 weeks prior to data collection. However, prior long-term training was not accounted for in the participant selection criteria and may have impacted performance in the mSEBT. While those currently engaging in single leg balance training or current competitive athletes were excluded, prior long-term dance training may have affected the outcome of the mSEBT (Kriyakiarana & Jongkamonwiwat, 2022). Two participants in the non-GJH group who had approximately 10 years of childhood ballet training showed the highest scores in MRD_{comp} and the highest MKA_{comp} of the non-GJH group. Though the training occurred at a young age, ballet training may have helped these participants feel more comfortable bending their knee more to

achieve further reaches. Other types of childhood exercise or balance training may have affected performance for GJH and non-GJH groups. Previous studies comparing different university sports teams found that soccer players, who perform and practice single leg balance when kicking a ball, performed better than athletes in other sports (Bressel et al., 2007; Stiffler et al., 2015). This observation likely indicates that type of athletic training affects MRD. Sports teams may have been homogenous groups in terms of prior training because they likely experienced similar training for a similar time period to achieve a sufficient level of skill for playing university-level sports. It may also be that type of physical activity may be more impactful than the number of MET-min on mSEBT performance. For example, Sabin and colleagues (2010) observed that non-athletes had higher MRD than basketball players. For this reason, lack of differences between groups in this study may be partially accounted for by comparing non-athletes to non-athletes. Future work should consider the participant's length and type of previous long term athletic, dance or balance training when evaluating outcomes of the mSEBT, though the thresholds that would be useful as exclusion criteria are unclear.

12.4.2 Measure of Physical Activity

Level of physical activity may have affected performance on the mSEBT. Although participants were excluded for self-reporting participation in more than 4 bouts of 30 minutes of structured exercise per week, there were eight participants who scored as outliers with more than a 960 MET-min/day or 16 MET-hours/day on the IPAQ. It is unclear if these eight participants over-reported their physical activity on the IPAQ (Sebastião et al., 2012). Outlier values on the IPAQ could also be a characteristic of the population. Gawel-Dabrowska et al. (2016) published boxplots of IPAQ scores of dentistry and medical students (n = 211; aged 23-29) showing means (~5,000 MET-min/week) and outliers comparable to those reported in this study. The presence of outliers in graduate and undergraduate university students may indicate that there is a more appropriate measure to capture physical activity engagement for this population than IPAQ.

12.4.4 Age

Participant age may have affected the presence of GJH-related symptoms in this sample. Symptoms of GJH progress with age but can be present in childhood (Castori et al., 2011). The oldest participant in this study, aged 34, was the only person who reported GJH symptoms as assessed by the BIoH. While there is no way to predict who with GJH will develop symptoms, it may be that clear biomechanical differences in dynamic balance and DKS may not be evident with younger and asymptomatic populations. The only study on disease progression suggests that diagnosis of symptomatic GJH becomes more complicated and less likely around the age of 33 (Castori et al., 2011). Additionally, given that 61-93% of adults diagnosed with symptomatic GJH have chronic fatigue and kinesiophobia, particularly in the “stiffness” phase of GJH which usually occurs in the third decade of life (Celletti et al., 2013; Kalisch et al., 2020; Rombaut et al., 2015), individuals with symptoms may be reluctant to participate in research studies involving exercise. Further, diagnosis of symptomatic GJH is delayed for an average of 14 years (Demmler et al., 2019). For these reasons, finding older participants with symptomatic GJH can be challenging. Nonetheless, recruiting people with GJH who are older and who have symptoms may be beneficial for future studies. When recruiting those with more symptoms, length of collection as well as type and duration of exercise should be considered to minimize participant burden.

12.5 Dynamic versus Static Balance

There may be no detectable biomechanical difference between those with asymptomatic GJH without GJH during dynamic balance. Like vertical jumping, dynamic balance on stable and unstable surfaces resulted in similar outcome and biomechanical measures as those without GJH. In terms of MRD_{comp} , the results of this study are consistent with Ewertowska et al. (2020), who found no difference in counter movement jump height between non-GJH and asymptomatic GJH groups. The results of MKA_{comp} are also consistent with Alsiri et al. (2020a) who found no difference in lower limb kinematics and kinetics between non-GJH and symptomatic GJH groups during vertical jumping. On the other hand, the lack of difference between groups in terms of $COPTe_{comp}$ is not in line with previous studies who

found increased COP excursion in static tasks (Bates et al., 2021c; Galli, Rigoldi, et al., 2011; Iatridou et al., 2014; Rombaut, Malfait, De Wandele, et al., 2011). The difference between this study's results and previous work may be the dynamic nature of the mSEBT compared to static tasks.

Differences between groups may be evident in lower limb joints not considered in this project. Knee joint angle was selected because previous work showed that the greatest difference between foam and no foam mSEBT performance is in knee flexion, MRD, centre of mass and COP (Nozu et al., 2021). Additionally, greater MRD is achieved through greater knee flexion, hip flexion or both knee and hip flexion (Robinson & Gribble, 2008). Since these differences in joint angles are accompanied by differences in MRD (Nozu et al., 2021), it is unlikely that there would be differences in ankle or hip angles between asymptomatic GJH and non-GJH in the current study. As demonstrated by Vermeulen and colleagues (2022), using a multi-segment foot model may reveal characteristics of GJH during movement. Vermeulen and colleagues (2022) observed increased foot eversion of the fore foot, increased dorsiflexion in the medial and lateral forefoot and increased inversion and abduction at the midfoot in symptomatic GJH versus non-GJH groups. Applying a multi segment foot model to the current study would have been complicated by marker occlusion in the foam condition.

A possible compensatory strategy not captured by this study is difference in muscle activation. Differences in muscle activation patterns in those with and without GJH have been observed (Jensen et al., 2013; Robbins et al., 2020; Schmid et al., 2013). It is possible that there were differences in muscle activation during the mSEBT that were not captured by the measures used in this study even though there were no between-groups differences in MRD_{comp} , MKA_{comp} and $COPTE_{comp}$.

13 Strengths

This study had several strengths. First, this study incorporated novel tasks, conditions, measures as well as the sampling of graduate and undergraduate university students with and without asymptomatic GJH. Recruitment in non-kinesiology departments expanded the scope of potential participants. Second, while other studies have recruited only female participants (Iatridou et al., 2014; Luder et al., 2015; Rombaut, Malfait, De Wandele, et al., 2011; Schmid et al., 2013), this is the first study to match participants on age and sex. Age and sex contribute to the severity of symptomatic GJH (Castori et al., 2013). Third, the careful set up of neutral knee alignment for the motion capture calibration trial ensured greater accuracy of kinematic data. Fourth, a range of biomechanical (kinetic and kinematic) and clinical (BS, disease impact, mSEBT) tools were used to ensure that laboratory data could be translated to clinical settings.

14 Limitations

The main limitations of this study are the absence of participants with symptomatic GJH and low sample size. Due to low prevalence (Hakim & Sahota, 2006; Kumar & Lenert, 2017) and delayed diagnosis (Demmler et al., 2019), there are very few people who have been diagnosed with symptomatic GJH. Without access to a patient group or GJH clinic, of which there are very few in Canada, and due to the timeline of this project, recruiting those with symptomatic GJH from a clinical setting was not possible. Additionally, excluding participants based on previous ankle sprain and level of physical activity may have further limited recruitment. Recruiting more symptomatic participants in conjunction with the sole Canadian EDS clinic and choosing a clinical test that did not exclude participants based on joint injury may help overcome these limitations.

In terms of sample size, the a priori sample size was chosen to reflect an appropriate scope, project timeline and the study visit duration. To determine the ideal sample size required for a difference between groups in this study, a post hoc power analysis was run on the primary dependent variable, MRD_{comp} ($n = 28$, $\eta^2 = 0.05$; Cohen's $d = 0.4$). Post hoc sample size estimate revealed a total sample of 164 (82 per group) (Figure 13), which is beyond the scope of this project. The substantially larger sample size of the post hoc sample size compared with a priori sample size and the range of sample sizes of most studies that found significant results with similar measures when observing GJH groups (12 – 32 participants), may indicate that there is no true difference between those with and without asymptomatic GJH in the current study (Bates & Alexander, 2015; Galli et al., 2011; Rigoldi et al., 2012; Rombaut, Malfait, De Wandele, et al., 2011). Conversely, it could indicate that larger sample sizes, like those used by Luder and colleagues (2015) ($n = 256$), may be required for biomechanical studies of this population.

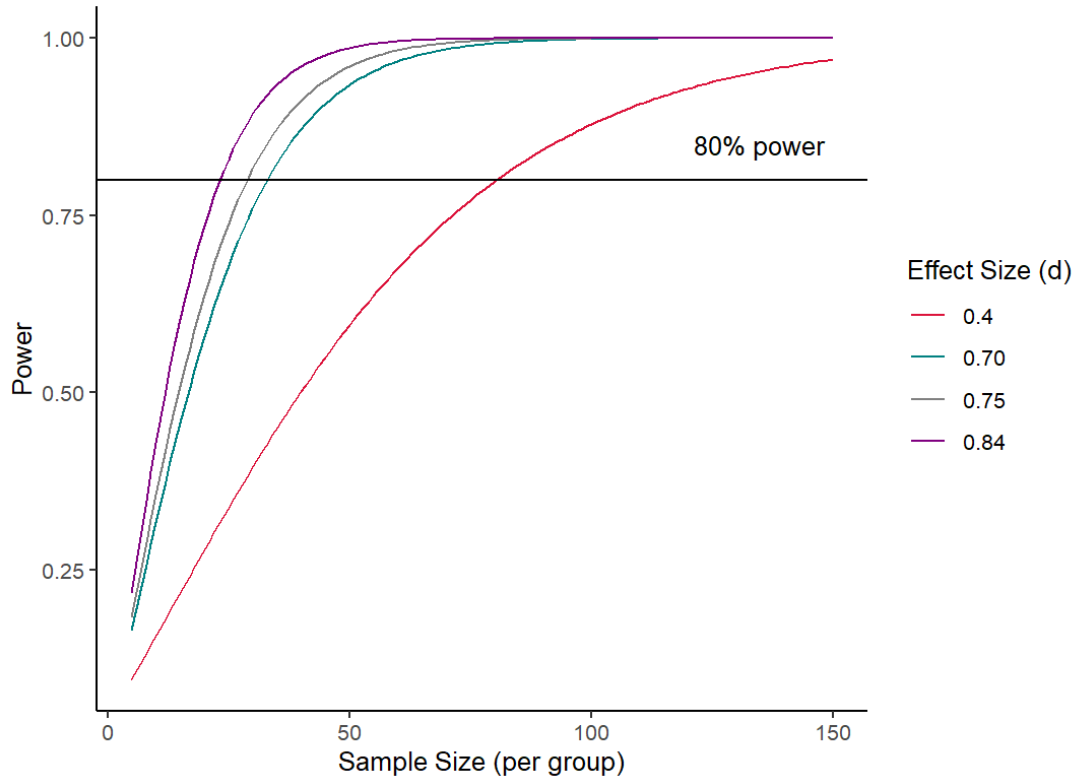


Figure 13. Power plot showing a priori and post hoc sample size estimation. A priori effect size as calculated from published data by Alsiri et al (2020) ($d = 0.7, 0.75, 0.84$) and effect size from the ANOVA run on composite MRD ($d = 0.4$). Post hoc sample size estimate is for a total sample of 164 (82 per group). All effect sizes are shown in Cohen's d ($d = \text{Cohen's } d$).

15 Future Work

The results of this study provide rationale for several potential options for future research. First, comparing the mSEBT between groups of those with symptomatic GJH and without GJH, following a group with symptomatic GJH over time, recruiting older participants, or recruiting based on GJH-specific symptoms may yield some understanding of the differences between symptomatic and asymptomatic GJH. These types of investigations could elucidate some information about age-based changes in dynamic balance. Second, an expansion of biomechanical measures and methods may be useful. For example, using EMG during the mSEBT may reveal some information about potential compensatory strategies used by those with GJH during dynamic balance tasks. Using a multi-segment foot model could also add a layer of complexity to modelling GJH which may be necessary for analysis of this population's biomechanics. Last, future work could investigate the interaction between physical activity and GJH. Such a study would account for type and duration of prior athletic or balance training and measure the possible association between physical activity, performance on dynamic tasks and symptom progression of GJH.

16 Conclusions

The mSEBT and DKS are not appropriate measures to differentiate between asymptomatic GJH and non-GJH groups in non-athlete university graduate and undergraduate students. There may be no detectable biomechanical differences in these samples, in part due to the absence of pain. Future work on the clinical use of the mSEBT and DKS may consider recruiting those with symptomatic GJH and/or older participants with GJH.

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DATE:

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Appendices**Appendix A: Participant Descriptor and Anthropometrics Data Collection Sheet****Race**

We aim to engage people of different races when studying health. Collecting this information helped us monitor and ensure diversity is represented in our studies.

We invite you to choose what best describes you (please **check all** that apply):

	Examples
<input type="checkbox"/> Black	African, Caribbean, Black Canadian, Afro-Latine, African American, or other African descent
<input type="checkbox"/> East Asian	Chinese, Korean, Japanese, or other East Asian descent
<input type="checkbox"/> Latine/Latinx	Latin American, Hispanic descent
<input type="checkbox"/> Middle Eastern	Afghan, Egyptian, Iranian, Lebanese, Turkish, Kurdish, or other Arab or Persian descent
<input type="checkbox"/> South Asian	East Indian, Pakistani, Bangladeshi, Sri Lankan, Indo-Caribbean, or other South Asian descent
<input type="checkbox"/> Southeast Asian	Filipino, Vietnamese, Cambodian, Thai, Malaysian, Indonesian, or other Southeast Asian descent
<input type="checkbox"/> White	British, German, Ukrainian, or other European descent
<input type="checkbox"/> Another race category	Not described above
<input type="checkbox"/> Do not know	
<input type="checkbox"/> Prefer not to answer	
<input type="checkbox"/> Prefer to self-describe	

If you chose "prefer to self-describe", please indicate your answer below:

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Sex and Gender

What is your sex assigned at birth?

- Prefer not to disclose
- Female
- Male
- Intersex
- Not listed

If you chose "not listed", please indicate your answer below:

What is your current gender identity?

- Prefer not to disclose
- Woman
- Man
- Non-binary
- Prefer to self-describe

If you chose "prefer to self-describe", please indicate your answer below:

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Anthropometrics and Date of Birth

Date of Birth (MM/DD/YYYY):	
Body Mass (kg):	
Height (m):	
BMI (kg/m ²)	
Leg length (cm):	Left:
	Right:
Dominant Leg:	<input type="checkbox"/> Left <input type="checkbox"/> Right

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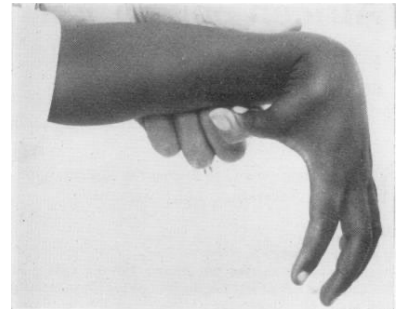
(MMM/DD/YYYY)

Appendix B: Beighton Criteria Collection Sheet

The following test protocol script for reproducibility of the Beighton Score is taken from Juul-Kristensen et al. (2007). Questions about historical JH were asked to maintain uniformity with this script but positive scores followed the guidelines in the diagnostic criteria which do not include questions about historical JH in BS testing.

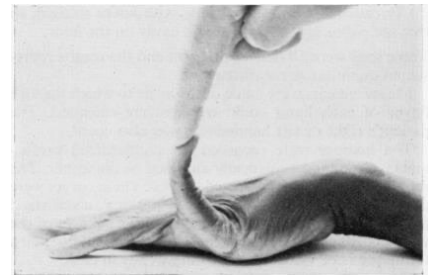
Photos of testing positions from Beighton et al. (1973).

1. Passive apposition of the thumb to the flexor side of the forearm (shoulder 90° flexed, elbow extended and hand pronated), tested on right and left side, is performed by the patient after the following procedure. The examiner performs the test and asks: 'Can you with a straight arm move your thumb down so it touches the lower part of the forearm?'



If the test is negative, meaning no touch, the examiner asks: 'Have you been able to do this previously?'

2. Passive dorsiflexion of the little finger >90° (elbow flexed 90°, the forearm and hand pronated resting on a table), tested on right and left side, is performed by the patient after the following procedure. The examiner performs the test and asks: 'Can you with the forearm resting on the table, move your little finger, so it is pointing a little bit backwards?'



If the test is negative, the examiner asks: 'Have you been able to do this previously?'

3. Passive hyperextension of the elbow >10° (shoulder 90° abducted and hand supinated), tested on right and left side, is performed by the patient after the following procedure. The examiner performs the test and asks: 'How much are you able to overstretch your elbow in this position (illustrated by the examiner) with your palm pointing towards the roof?'



If the test is negative, meaning no overstretch, the examiner asks: 'Have you been able to overstretch the elbow previously?'

4. Passive hyperextension of the knee >10° (standing), tested on right and left side, is performed by the patient after the following procedure. The examiner performs the test and asks: 'How much are you able to overstretch your knee when you are standing straight up?'



If the test is negative, meaning no overstretch, the examiner asks: 'Have you been able to overstretch the knee previously?'

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5. Forward flexion of the trunk, with knees straight, so that the palms of the hands rest easily on the floor, is performed by the patient after the following procedure. The examiner performs the test and asks: 'Can you with straight knees bend your body forward and place both palms easily on the ground?'

If the test is negative, meaning no touch on the ground with the whole palm of the hands, the examiner asks: 'Have you been able to do this previously?'



Specific Joint Hypermobility	YES	NO
1. Passive apposition of the thumb to forearm on flexor side of the forearm (shoulder 90° flexed, elbow extended and hand pronated),	<input type="checkbox"/> LEFT <input type="checkbox"/> RIGHT	<input type="checkbox"/>
2. Passive dorsiflexion of the little finger >90° (elbow flexed 90°, the forearm and hand pronated resting on a table)	<input type="checkbox"/> LEFT <input type="checkbox"/> RIGHT	<input type="checkbox"/>
3. Passive hyperextension of the elbow >10° (shoulder 90° abducted and hand supinated)	<input type="checkbox"/> LEFT <input type="checkbox"/> RIGHT	<input type="checkbox"/>
4. Passive hyperextension of the knee >10° (standing)	<input type="checkbox"/> LEFT <input type="checkbox"/> RIGHT	<input type="checkbox"/>
5. Forward flexion of the trunk, with knees straight, so that the palms of the hands rest easily on the floor	<input type="checkbox"/> LEFT <input type="checkbox"/> RIGHT	<input type="checkbox"/>
Total	/9	

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Appendix C: The Five-Part Questionnaire for Identifying Hypermobility

Please check one answer per question:

	Yes	No
1. Can you now (or could you ever) place your hands flat on the floor without bending your knees?		
2. Can you now (or could you ever) bend your thumb to touch your forearm?		
3. As a child, did you amuse your friends by controlling your body into strange shapes or could you do the splits?		
4. As a child or teenager, did your shoulder or kneecap dislocate on more than one occasion?		
5. Do you consider yourself double-jointed?		

*Answering “yes” to 2 or more suggests symptomatic JH with 84% sensitivity and 80-89% specificity

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Appendix D: Bristol Impact of Hypermobility Questionnaire (for the General Public)**BIOH QUESTIONNAIRE - Adapted for the General Public**

This questionnaire is designed to ask how your general health affects your day to day life. Please answer all of the questions and try not to think too much about your answer.

A. **During the past 7 days**, have you had pain in any of the following areas?

	Yes	No
Shoulders	<input type="checkbox"/>	<input type="checkbox"/>
Elbows	<input type="checkbox"/>	<input type="checkbox"/>
Wrists	<input type="checkbox"/>	<input type="checkbox"/>
Hands	<input type="checkbox"/>	<input type="checkbox"/>
Hips	<input type="checkbox"/>	<input type="checkbox"/>
Knees	<input type="checkbox"/>	<input type="checkbox"/>
Ankles	<input type="checkbox"/>	<input type="checkbox"/>
Feet	<input type="checkbox"/>	<input type="checkbox"/>
Neck	<input type="checkbox"/>	<input type="checkbox"/>
Back	<input type="checkbox"/>	<input type="checkbox"/>

B. We would like to know how often you have experienced pain and fatigue during the **past 7 days**.

Please circle the number which best reflects...your **average** level of pain during the **past 7 days**

1)	0	1	2	3	4	5	6	7	8	9	10	
	No pain										Worst imaginable pain	
2)	your worst level of pain during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	No pain										Worst imaginable pain	
3)	how much pain you have had when walking during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	No pain										Worst imaginable pain	
4)	how much pain you have had when resting during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	No pain										Worst imaginable pain	
5)	your average level of fatigue during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	No fatigue										Totally exhausted	
6)	the effect fatigue has had on your life during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	No effect										Large effect	
7)	how well you have coped with fatigue during the past 7 days											
	0	1	2	3	4	5	6	7	8	9	10	
	Not at all well										Very well	

*Reverse scored (0=10, 1=9, etc)

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- C. Please tick the box which best describes how much, during the **past 7 days**, your general health has affected...

	Not at all ¹	A little ²	Somewhat ³	A lot ⁴	Completely ⁵
8) the footwear you have worn	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9) the transport you have used	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- D. **How often.....**

	Never ¹	Occasionally ²	Sometimes ³	Often ⁴	Always ⁵
10) have you had unexpected pain (that was not an expected consequence of something you have done) during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11) has your wrist or hand given way, leading you to drop, or nearly drop something during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12) has your ankle, knee or hip given way, leading to a stumble or trip during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13) have you lost your balance during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14) have joints seized up during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15) has it felt like a joint has slipped out of place during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16) have you had muscle cramps or spasms during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17) has your sleep been disturbed due to pain or discomfort during the past 7 days?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

/50

- E. How much difficulty have you had with the following tasks during the **past 7 days**?

	Not difficult ¹	A little difficult ²	Somewhat difficult ³	Extremely difficult ⁴	Completely impossible ⁵
18) Bending or twisting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
19) Squatting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
20) Walking on uneven ground	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
21) Carrying a heavy bag, such as a shopping bag	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
22) Reaching up to high shelves	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
23) Pulling or pushing heavy doors	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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24) Opening a tight or new jar

	Not difficult ¹	A little difficult ²	Somewhat difficult ³	Extremely difficult ⁴	Completely impossible ⁵
--	----------------------------	---------------------------------	---------------------------------	----------------------------------	------------------------------------

25) Writing for more than 30 minutes 26) Peeling or chopping vegetables 27) Carrying a saucepan full of water F. How much discomfort would you have had after the following activities **during the past 7 days?**

	No discomfort ¹	Slightly uncomfortable ²	Uncomfortable ³	Painful ⁴	Could not do it ⁵
--	----------------------------	-------------------------------------	----------------------------	----------------------	------------------------------

28) Standing up for more than 30 minutes 29) Sitting in a chair for more than 30 minutes 30) Standing up after sitting for more than 30 minutes 31) Climbing several flights of stairs 32) Going down several flights of stairs 33) Walking at your own pace for a few miles 34) Walking briskly for a few miles 35) Wandering around shops or museums 36) Bending or twisting 37) Squatting G. **Please circle** the number which best indicates...38) how much you have felt in control of the movement of your body and limbs during the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10

Completely in control

Completely unable to control

39) how accurately you have been able to predict how you might feel in general over the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10

Always able to predict

Completely unable to predict

40) how frustrated you have felt with your general health during the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10

Not at all frustrated

Very frustrated

41) how strong your body and limbs have felt generally over the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10

Very strong

Extremely weak

42) how 'tight', 'strong', 'held together' your body and limbs have felt generally during the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10
Very tight Extremely loose

43) how able you have felt to control your fatigue in the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10
Completely in control No control whatsoever

44) how much you have felt in control of your pain in the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10
Completely in control No control whatsoever

45) how much you have felt in control of your life in the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10
Completely in control No control whatsoever

H. Thinking about what you are usually able to do, how much has your general health interfered with your activities during the **past 7 days**?

Please circle the number which best shows. . .

46) how much your general health has interfered with your daily activities during the **past 7 days**?

0 1 2 3 4 5 6 7 8 9 10
Not at all Unable to do

47) how much difficulty you have had in carrying out your desired level of exercise during the **past 7 days**

0 1 2 3 4 5 6 7 8 9 10
No difficulty Extreme difficulty

I. Please tick the box which best describes your agreement with the following statements

		Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly disagree
48)	My body does not feel strong	<input type="checkbox"/> ⁵	<input type="checkbox"/> ⁴	<input type="checkbox"/> ³	<input type="checkbox"/> ²	<input type="checkbox"/> ¹
49)	I am concerned about my general health getting worse	<input type="checkbox"/> ⁵	<input type="checkbox"/> ⁴	<input type="checkbox"/> ³	<input type="checkbox"/> ²	<input type="checkbox"/> ¹
50)	I feel frustrated with my general health	<input type="checkbox"/> ⁵	<input type="checkbox"/> ⁴	<input type="checkbox"/> ³	<input type="checkbox"/> ²	<input type="checkbox"/> ¹
51)	My coordination is poor	<input type="checkbox"/> ⁵	<input type="checkbox"/> ⁴	<input type="checkbox"/> ³	<input type="checkbox"/> ²	<input type="checkbox"/> ¹
52)	I feel that I could trip or fall at any time	<input type="checkbox"/> ⁵	<input type="checkbox"/> ⁴	<input type="checkbox"/> ³	<input type="checkbox"/> ²	<input type="checkbox"/> ¹
53)	I can control the movement of my limbs	<input type="checkbox"/> ¹	<input type="checkbox"/> ²	<input type="checkbox"/> ³	<input type="checkbox"/> ⁴	<input type="checkbox"/> ⁵
54)	I feel that I can remain physically active	<input type="checkbox"/> ¹	<input type="checkbox"/> ²	<input type="checkbox"/> ³	<input type="checkbox"/> ⁴	<input type="checkbox"/> ⁵
55)	I feel that I can manage my general health	<input type="checkbox"/> ¹	<input type="checkbox"/> ²	<input type="checkbox"/> ³	<input type="checkbox"/> ⁴	<input type="checkbox"/> ⁵

/40

Thank you for taking the time to complete this questionnaire.

Total

/360

Appendix E: International Physical Activity Questionnaire (Long Version)

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health-related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an *International Physical Activity Prevalence Study* is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

Yes

No →

Skip to PART 2: TRANSPORTATION

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ **days per week**

No vigorous job-related physical activity



Skip to question 4

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

No moderate job-related physical activity



Skip to question 6

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

No job-related walking



Skip to PART 2: TRANSPORTATION

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

No traveling in a motor vehicle



Skip to question 10

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**

_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

No bicycling from place to place



Skip to question 12

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ hours per day
_____ minutes per day

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ days per week

No walking from place to place



***Skip to PART 3: HOUSEWORK,
HOUSE MAINTENANCE, AND
CARING FOR FAMILY***

13. How much time did you usually spend on one of those days walking from place to place?

_____ hours per day
_____ minutes per day

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ days per week

No vigorous activity in garden or yard



Skip to question 16

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**

_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

No moderate activity in garden or yard



Skip to question 18

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**

_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

No moderate activity inside home



***Skip to PART 4: RECREATION,
SPORT AND LEISURE-TIME
PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**

_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

No walking in leisure time



Skip to question 22

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**

_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

No vigorous activity in leisure time



Skip to question 24

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

No moderate activity in leisure time



Skip to PART 5: TIME SPENT SITTING

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**

_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**

_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Appendix G: Modified Star Excursion Balance Test Randomization

Trials were counterbalanced according to the following notation:

Conditions	Directions	Starting leg
1 = No foam	4 = Anterior	7 = Dominant
2 = Foam	5 = Posterolateral	8 = Non-dominant
3 = Timed	6 = Posteromedial	

Randomized order of testing:

Set	Participant ID	Condition			Direction			Leg order	
1	H_01	3	1	2	4	5	6	7	8
2	H_02	3	1	2	6	4	5	8	7
3	H_03	2	3	1	5	6	4	8	7
4	H_04	1	3	2	6	4	5	7	8
5	H_05	1	3	2	6	5	4	8	7
6	C_01	1	3	2	5	4	6	7	8
7	C_02	3	2	1	4	6	5	7	8
8	C_03	1	2	3	5	6	4	7	8
9	C_04	2	3	1	5	6	4	7	8
10	C_05	1	2	3	5	4	6	7	8
11	H_06	3	2	1	5	6	4	8	7
12	H_07	1	2	3	4	5	6	8	7
13	H_08	3	2	1	6	5	4	7	8
14	H_09	2	3	1	4	6	5	7	8
15	H_10	3	1	2	6	5	4	8	7
16	C_06	1	3	2	4	6	5	7	8

17	C_07	1	2	3	4	5	6	7	8
18	C_08	3	2	1	4	5	6	8	7
19	C_09	2	3	1	5	4	6	7	8
20	C_10	2	1	3	6	4	5	8	7
21	H_11	2	1	3	5	6	4	8	7
22	H_12	2	3	1	5	4	6	7	8
23	H_13	2	1	3	4	5	6	7	8
24	H_14	2	1	3	4	6	5	8	7
25	H_15	2	3	1	6	5	4	7	8
26	C_11	1	3	2	4	6	5	7	8
27	C_12	2	3	1	5	6	4	7	8
28	C_13	2	1	3	4	6	5	7	8
29	C_14	2	3	1	4	5	6	7	8
30	C_15	3	2	1	5	6	4	7	8
31	C_16	1	2	3	5	6	4	7	8
32	C_17	1	2	3	5	4	6	7	8

Appendix H: Descriptors and Dependent Variables by Participant

Table 8. Descriptors by participant.

P	Group	Dom leg	Sex	Age	BMI	BS (/9)	BIoH	IPAQ	NPRS (/11)	Gait speed (m/s)
H_01	GJH	R	F	30	23.25	5	65	15039	0	1.2
H_02	GJH	R	F	24	19.18	9	98	2395.5	2.5	1.2
H_03	GJH	R	F	25	22.6	7	67	3501	0	1.3
H_04	GJH	R	F	23	29.5	8	169	9445	0.5	1.3
H_05	GJH	R	F	27	29.6	5	109	806	0	1.3
H_06	GJH	R	F	21	18.85	5	121	2841	0	1.3
H_07	GJH	R	F	18	22.4	7	59	770	0	1.2
H_08	GJH	R	F	34	36.7	6	239	4470	1	1.2
H_09	GJH	R	F	25	24.8	7	118	2188	0	1.2
H_10	GJH	R	F	23	19.2	5	110	4528	0	1.3
H_11	GJH	R	F	26	24.8	6	89	2378	0	1.3
H_12	GJH	R	F	27	21.5	6	90	4048	0	1.1
H_13	GJH	R	M	21	25.4	5	111	9348	0	1.2
H_14	GJH	R	F	20	20.1	6	60	1885.5	0	1.1
C_01	Non-GJH	R	F	19	26.06	2	67	5851.5	0	1.1
C_02	Non-GJH	R	F	31	23.88	1	54	2816	0	1.4
C_04	Non-GJH	R	F	20	19.8	0	80	7344	0	1.3
C_06	Non-GJH	R	F	25	16.9	1	104	3534	0	1.3
C_07	Non-GJH	R	F	23	21.8	0	57	12321	0	1.2
C_08	Non-GJH	R	F	25	22.7	1	102	3331	0	1.4
C_09	Non-GJH	R	F	30	21	0	44	8738	0	1.4
C_10	Non-GJH	R	F	30	25	2	89	786.5	0	1.1
C_11	Non-GJH	R	F	24	20.9	4	52	3472	0	1.2
C_12	Non-GJH	R	F	26	19.2	0	73	4023	0	1.2
C_13	Non-GJH	R	F	22	29.3	3	106	9018	0	1.0
C_15	Non-GJH	R	F	20	28.6	0	114	1902	0	1.3
C_16	Non-GJH	L	M	21	28.4	0	40	2856	0	1.4
C_17	Non-GJH	R	F	30	26.1	0	116	10272	1	1

Gait speed indicates self-selected pace. Abbreviations: P = participant; GJH = Generalized Joint Hypermobility, Dom leg = dominant leg, F = female, M = male, BMI = Body Mass Index, IPAQ = International Physical Activity Questionnaire, BS = Beighton Score, BIoH = Bristol Impact of Hypermobility Questionnaire, NRPS = Numeric Pain Rating Scale (difference between before and after dynamic balance testing).

Table 9. Beighton score count by joint assessed and group.

Group	Total (n=28)	Non-GJH (n=14)	GJH (n=14)
Left 1st MT	10	1	9
Right 1st MT	11	1	10
Left 5th MT	10	0	10
Right 5th MT	9	0	9
Left Elbow	13	2	11
Right Elbow	12	3	9
Left Knee	15	3	12
Right Knee	13	3	10
Spine	8	1	7

Abbreviations: GJH = Generalized Joint Hypermobility, MT = metatarsal.

Table 10. Maximum Reach Distance by participant.

Participant	Group	MRD_{comp}	No Foam	Foam	Timed
H_01	GJH	81.4	76.57	89.21	78.39
H_02	GJH	76.8	75.87	78.44	76.17
H_03	GJH	81.5	81.54	83.40	79.50
H_04	GJH	76.9	77.02	81.31	72.43
H_05	GJH	82.3	82.80	85.45	78.65
H_06	GJH	88.8	90.15	89.33	86.97
H_07	GJH	82.1	81.31	83.71	81.43
H_08	GJH	75.3	74.80	76.35	74.81
H_09	GJH	68.6	68.77	68.96	68.17
H_10	GJH	78.5	77.80	80.35	77.35
H_11	GJH	78.8	78.19	81.29	76.98
H_12	GJH	71.4	70.86	73.74	69.48
H_13	GJH	92.9	93.61	97.60	87.38
H_14	GJH	69.2	69.55	71.59	66.56
C_01	Non-GJH	75.2	72.3	79.6	73.9
C_02	Non-GJH	76.1	75.0	79.2	74.1
C_04	Non-GJH	70.6	70.2	70.0	71.6
C_06	Non-GJH	81.3	79.5	84.1	80.2
C_07	Non-GJH	71.6	71.4	71.5	71.8
C_08	Non-GJH	90.0	90.1	91.5	88.4
C_09	Non-GJH	77.7	77.0	77.7	78.3
C_10	Non-GJH	67.4	67.2	68.0	67.0
C_11	Non-GJH	71.1	67.5	69.1	64.2
C_12	Non-GJH	86.1	86.1	86.5	85.8
C_13	Non-GJH	76.9	78.3	79.3	73.1
C_15	Non-GJH	77.8	78.0	80.6	74.6
C_16	Non-GJH	80.8	82.0	84.1	76.3

C_17	Non-GJH	61.7	61.7	61.6	61.8
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Abbreviations: GJH = Generalized Joint Hypermobility, MRD_{comp} = Maximum Reach Distance composite score.

Table 11. Center of Pressure Total Excursion by participant.

Participant	Group	COPTE_{comp}	No Foam	Foam	Timed
H_01	GJH	29.23	27.43	26.37	33.89
H_02	GJH	32.31	31.04	31.47	34.42
H_03	GJH	31.89	32.06	32.14	31.47
H_04	GJH	42.23	38.33	43.50	44.85
H_05	GJH	24.97	26.39	25.28	23.23
H_06	GJH	39.22	33.28	46.48	37.89
H_07	GJH	28.54	23.40	25.41	36.80
H_08	GJH	36.24	34.24	34.70	39.79
H_09	GJH	21.29	14.00	16.72	33.16
H_10	GJH	16.82	15.40	17.34	17.73
H_11	GJH	29.01	25.37	26.51	35.16
H_12	GJH	34.62	36.73	31.51	35.61
H_13	GJH	48.12	54.65	57.90	31.82
H_14	GJH	26.04	22.26	25.12	30.75
C_01	Non-GJH	46.22	44.40	46.29	47.95
C_02	Non-GJH	33.44	30.40	36.48	n/a
C_04	Non-GJH	18.57	15.98	16.19	23.53
C_06	Non-GJH	31.01	17.82	40.98	34.24
C_07	Non-GJH	20.66	n/a	17.39	23.94
C_08	Non-GJH	43.17	42.29	49.34	37.87
C_09	Non-GJH	18.81	13.79	18.50	24.14
C_10	Non-GJH	21.71	17.88	22.18	25.07
C_11	Non-GJH	31.54	22.48	36.36	35.77
C_12	Non-GJH	32.60	28.53	32.24	37.04
C_13	Non-GJH	35.78	34.97	26.29	46.09
C_15	Non-GJH	38.65	42.47	37.48	36.01
C_16	Non-GJH	32.43	31.30	32.29	33.70
C_17	Non-GJH	27.08	21.48	15.16	44.61

Abbreviations: GJH = Generalized Joint Hypermobility, COPTE_{comp} = Center of Pressure Total Excursion composite score.

Table 12. Maximum Knee Flexion Angle by participant.

Participant	Group	MKA_{comp}	No Foam	Foam	Timed
H_01	GJH	50.39	52.48	42.49	56.19
H_02	GJH	56.64	57.26	57.47	55.18
H_03	GJH	52.45	52.87	53.43	51.06
H_04	GJH	42.80	48.34	41.01	39.05

H_05	GJH	50.71	54.13	48.67	49.33
H_06	GJH	60.72	64.62	61.07	56.46
H_07	GJH	41.33	40.75	43.35	39.89
H_08	GJH	53.03	54.55	52.27	52.28
H_09	GJH	45.24	48.69	46.87	40.17
H_10	GJH	45.84	43.51	49.68	44.35
H_11	GJH	51.32	51.22	52.49	50.26
H_12	GJH	48.19	50.38	46.97	47.22
H_13	GJH	62.18	67.76	58.02	60.76
H_14	GJH	50.09	51.68	47.42	51.18
C_01	Non-GJH	33.47	39.56	38.73	22.13
C_02	Non-GJH	51.59	53.57	50.35	50.84
C_04	Non-GJH	42.99	37.99	50.71	40.28
C_06	Non-GJH	58.40	56.92	60.05	58.24
C_07	Non-GJH	58.61	59.55	61.11	55.18
C_08	Non-GJH	43.21	39.60	51.04	39.01
C_09	Non-GJH	46.95	44.78	49.61	46.46
C_10	Non-GJH	39.17	38.89	39.33	39.29
C_11	Non-GJH	39.94	42.18	38.46	39.17
C_12	Non-GJH	56.33	55.08	59.53	54.38
C_13	Non-GJH	50.28	54.16	48.35	48.34
C_15	Non-GJH	61.46	62.52	62.60	59.27
C_16	Non-GJH	55.55	59.05	53.13	54.47
C_17	Non-GJH	42.23	33.96	45.10	47.61

Abbreviations: GJH = Generalized Joint Hypermobility, MKA_{comp} = Maximum Knee Flexion Angle composite score.

Table 13. Normalized and non-normalized Dynamic Knee Stiffness by participant in the non-dominant leg.

Participant	Group	DKS (timed)		DKS (untimed)	
		Nm/kg/°	Nm/°	Nm/kg/°	Nm/°
H_01	GJH	0.03	2.01	0.04	2.79
H_02	GJH	0.03	2.20	0.05	3.10
H_03	GJH	0.11	7.09	0.15	9.47
H_04	GJH	0.09	5.41	0.10	5.60
H_05	GJH	0.03	2.24	0.05	3.50
H_06	GJH	0.05	2.59	0.10	5.55
H_07	GJH	0.05	3.44	0.06	4.23
H_08	GJH	0.04	4.24	0.07	7.60
H_09	GJH	0.07	4.76	0.08	5.34
H_10	GJH	0.06	3.02	0.03	1.65
H_11	GJH	0.04	3.02	0.07	4.49
H_12	GJH	n/a	n/a	n/a	n/a

H_13	GJH	0.04	3.00	0.05	4.26
H_14	GJH	0.04	2.72	0.04	2.71
C_01	Non-GJH	0.06	4.43	0.08	5.86
C_02	Non-GJH	0.11	6.06	0.13	6.86
C_04	Non-GJH	0.05	2.79	0.06	3.35
C_06	Non-GJH	0.08	3.85	0.08	3.67
C_07	Non-GJH	0.13	7.10	0.13	7.65
C_08	Non-GJH	0.03	2.17	0.06	4.09
C_09	Non-GJH	0.03	1.76	0.05	2.80
C_10	Non-GJH	0.04	2.59	0.03	2.04
C_11	Non-GJH	0.07	4.79	0.09	5.94
C_12	Non-GJH	0.06	3.07	0.08	3.91
C_13	Non-GJH	0.05	3.87	0.02	1.46
C_15	Non-GJH	0.07	5.03	0.09	6.57
C_16	Non-GJH	0.06	5.55	0.06	5.64
C_17	Non-GJH	0.06	3.99	0.06	4.05

Timed indicates normalized speed of 1.0m/s, untimed indicates self-selected speed. Normalized scored as in Nm/kg/°. Non-normalized scores are in Nm/°. Abbreviations: GJH = Generalized Joint Hypermobility, DKS = Dynamic Knee stiffness.