Understanding the psychosocial impact of Joint Hypermobility and Ehlers-Danlos Syndromes

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Abstract

Introduction: Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT) are heritable disorders affecting connective tissue. Existing research has predominately focused on biological features such as joint range of movement and pain, while less consideration has been given to psychosocial and behavioural factors.

Methods: This multiphase mixed-methods design explored the lived experience of adults with JHS and EDS in three studies. Firstly, a systematic review of the literature appraised and analysed nine papers using thematic synthesis. Secondly, semi-structured telephone interviews with a purposive sample of 17 adults (14 women, 3 men), considered participants' lived experiences and the psychosocial, cognitive and behavioural impact of JHS/EDS-HT on their lives. In the final study, these results were mapped to the Theoretical Domains Framework and COM-B model in a behavioural analysis to identify potential behaviour change interventions. Intervention options were presented to focus group participants (n=9, all women) with JHS/EDS-HT to gain consensus on priorities in a modified nominal group technique (NGT).

Results: Results from the systematic review showed that people with JHS and EDS experience difficulties being understood by others in society, have limited participation in social activities, and often depend on their families for help. Similarly, results from interviews indicated a general lack of awareness of JHS/EDS-HT, fears regarding injuries or decline in ability, and a range of positive coping strategies including physiotherapy. The behavioural analysis prioritised a number of different behaviour change interventions.

Conclusion: The psychosocial impact of JHS/EDS-HT on adults is substantial, and there are a number of unmet areas of care and support for this population. Novel findings have been linked to potential intervention recommendations. The findings

are discussed and triangulated in relation to existing literature and implications for future research.

Table of contents

Tables and figures

1. Chapter 1: Thesis overview

This PhD provides an in-depth exploration and understanding of the lived experience, psychosocial, cognitive and behavioural impact of Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT) using a qualitatively driven mixed-methods design. These qualitative results will be used to identify barriers to the effective self-management of JHS/EDS-HT using behaviour change theory; the Theoretical Domains Framework (TDF) and capability, opportunity, motivation-behaviour model (COM-B; Michie *et al.,* 2015). Recommendations for an innovative and theoretically driven behaviour change intervention will be then be prioritised by adults with JHS/EDS-HT to encourage improved self-management of their condition. This introductory chapter will provide a brief overview of JHS/EDS-HT, its associated psychosocial factors, and the lack of current options (National Health Service (NHS), or best practice guidance) regarding treatment and patient outcomes. Lastly, the overall aims of the PhD and the chapter structure are discussed.

1.1 Joint Hypermobility and Ehlers-Danlos Syndromes

JHS and EDS-HT are heritable disorders of connective tissue thought to be due to a genetic defect in the production of collagen, however the exact defects responsible have yet to be identified in the hypermobile subtype of the syndrome (Malfait *et al.*, 2017). Connective tissue acts as the body's 'glue', supporting and binding together a range of internal structures (Dorland, 2011). The primary clinical features are due to varying degrees of tissue fragility of the skin, ligaments, blood vessels and body tissues (Callewaert *et al.*, 2008). Symptoms can be broad and wide-ranging and include joint instability, recurrent dislocations, increased range of movement, easy bruising and joint pain (Hakim and Grahame, 2003). Increased incidences of fibromyalgia (Acasuso-Diaz and Collantes-Estevez, 1998), muscle weakness, (Voermans *et al.*, 2010) and poor postural control (Galli *et al.*, 2011) have also been reported. In addition, due to the 'whole body' nature of connective tissue, severe symptoms have been associated in other body systems, including

cardiovascular, autonomic (Gazit *et al.*, 2003), urinary (Arunkalaivanan *et al.*, 2009) and gastrointestinal systems (Fikree *et al.*, 2014).

Generalised joint hypermobility (GJH), or joints that move beyond a normal range of motion is one of the most prominent features of JHS/EDS-HT. Hypermobility can be assessed using the Beighton Score (detailed below). A score is obtained by assessing a series of lower limb, upper limb and spinal movements performed by the patient:

1) Forward flexion of the trunk with knees fully extended, so that the palms of the hand rest flat on the floor; one point.
2) Hyperextension of the elbows beyond 10^{o}; one point for each elbow.
3) Hyperextension of the knees beyond 10^{o}; one point for each knee.
4) Passive apposition of the thumbs to the flexor aspect of the forearm; one point for each hand.
5) Passive dorsiflexion of the 5th metocarpophalangeal joint beyond 90^{o}; one point for each hand.

There has been great variation historically regarding cut-off points in order to meet the diagnostic criteria for GJH, from ≥4/9 in the Brighton criteria (Grahame *et al.*, 2000), ≥5/9 in the Villefranche criteria (Beighton *et al.*, 1998), to ≥8/9 suggested in a study of Swedish schoolchildren (Jansson *et al.*, 2004).

Although some have argued that the range of joints tested using the Beighton score are limited (Russek, 2000) and may not correlate with the severity of a patient's pain (Grahame *et al.*, 2000), the Beighton Score has been tested and found to be a comparable measurement of hypermobility in both adults (Boyle *et al.*, 2003) and children (Smits-Engelsman *et al.*, 2013). The Beighton score is critically evaluated in the next chapter.

Before reclassification in 2017 (Malfait *et al.*, 2017), EDS had six main subtypes (with the most common Hypermobility Type (EDS-HT, formerly Type III) considered to be the same as JHS; the terms are used interchangeably throughout the literature (Tinkle *et al.*, 2009). The subtypes of EDS vary in genetic heritability and clinical severity, with types such as Classical EDS involving hypermobility of small

joints and easy bruising, to Vascular EDS, which due to notable fragility of tissues and organs, can result in arterial rupture and death, and has a limited life expectancy of 48 years, on average (Pepin *et al.*, 2000). The hypermobility subtype of EDS (EDS-HT) is the most common, and is the focus of this research.

The international classification for Ehlers-Danlos Syndromes was revised in 2017, with the terms Hypermobile Ehlers-Danlos Syndrome (hEDS), and Hypermobility Spectrum Disorder (HSD), replacing Ehlers-Danlos Hypermobility Type (EDS-HT) and Joint Hypermobility Syndrome (JHS) respectively (Malfait *et al.*, 2017). During the course of data collection for this PhD, the revised 2017 nosology had yet to been published. Although later stages of data collection were conducted after the changes to the diagnostic criteria, all participants had been diagnosed prior to the changes in terminology. To ensure consistency and prevent confusion, this thesis will use the combined term JHS/EDS-HT, except where authors have used one term specifically.

In a UK musculoskeletal triage service JHS was found to affect 30% of all those screened (Connelly, 2015). Literature specifically relating to all EDS subtypes estimates a frequency of approximately 1 in 5000 (Royce and Steinmann, 2003). However, the actual prevalence of either JHS or EDS-HT within the population has yet to be conclusively studied and historical and geographical variations in diagnostic criteria and nosology for JHS and EDS-HT have made comparing research difficult (Castori, 2012).

JHS/EDS-HT has been associated with a substantial psychological impact, including increased stress and anxiety and depression, (Scheper *et al.*, 2016, Smith *et al.*, 2014b). Qualitative literature in this area is minimal, but has indicated that patients with JHS/EDS-HT typically took many years to be diagnosed; that recognition of the condition is poor in primary care, and patients have frequently reported feeling misunderstood by friends, family and healthcare professionals (Berglund *et al.*, 2010, Palmer *et al.*, 2016a, Schmidt *et al.*, 2015). However, as later chapters of this thesis will identify, there has been very little research in the UK, and of these, the majority of studies used small sample sizes or focus groups (Palmer *et al.*, 2016b, Schmidt *et al.*, 2015). There is scope for enhanced understanding of patients' day-to-day lived experience of their JHS/EDS-HT, and its associated

psychological, cognitive and behavioural influences, using more sensitive and patient-focused measures, such as semi-structured interviews.

There are further challenges for people with JHS/EDS-HT, compared to other musculoskeletal conditions. At present, even if patients manage to receive an accurate JHS/EDS-HT diagnosis there is a lack of treatment guidance and patient education in the UK. Compared to the substantial literature and recommendations for patient education and self-management for other musculoskeletal conditions such as inflammatory or degenerative arthritis (National Institute for Health and Care Excellence, 2018), there is very little recognition and patient support for this condition.

There is an unmet need for researchers and clinicians to have a greater understanding of the impact of JHS/EDS-HT (Berglund and Nordstrom, 2001, Rombaut *et al.*, 2011a). Although quantitative research has demonstrated significantly higher rates of depression, anxiety, agoraphobia, panic disorder and low quality of life in this population (Smith *et al.*, 2014b), without robust, high-quality qualitative research with patients, we will not know which factors or which elements of the multisystemic nature of the condition are impacting patients' lives in such a significant way. By thoroughly understanding the complex impact of JHS/EDS-HT on patients' lives, we can develop more effective, targeted management options.

Lastly, there has yet to be any research with this population exploring how to overcome the barriers identified by participants in daily life. Poorly managed chronic pain and recurrent injury are very common in JHS/EDS-HT and can be significantly disabling (Castori *et al.*, 2010, Grahame, 2009). Poorly managed chronic pain has been shown to lead to fear of movement and catastrophising responses to symptoms, leading to muscle deconditioning, fear of injury and pain (Hakim *et al.*, 2017), potentially leading to an over-reliance on emergency care. Described as a physical and psychological decline in the JHS/EDS-HT literature, poorly managed symptoms can lead to substantial emotional costs such as low confidence, anxiety, depression and social isolation (Grahame, 2009).

By using patient-preferred methods and input from key stakeholders, we can develop a comprehensive self-management intervention to encourage patients to better self-manage and control their own condition. Self-management can be

defined as a person's ability to manage the symptoms, treatments, physical and psychological consequences and lifestyle changes associated with living with a chronic condition (Barlow *et al.*, 2002), p.178). Improved holistic self-management can lead to many positive outcomes for patients, and potentially improve patient care for this population in the long-term.

1.2 Aims:

Specific objectives have been detailed within each chapter. The overarching aims of this thesis are:

- To understand the lived experiences of people with JHS and EDS
- To explore the psychosocial, cognitive and behavioural impact of JHS/EDS-HT.
- To determine the components of a self-management behaviour change intervention for people with JHS/EDS-HT.

1.3 Thesis outline

1.3.1 Chapter Two: Background

This background chapter gives an overview of the diagnostic criteria, treatment and associated psychological symptoms. Recent changes to the JHS/EDS-HT diagnostic criteria in 2017 have been outlined and critically evaluated. Prevalence of generalised joint hypermobility (GJH), and Joint Hypermobility Syndrome (JHS) in adults, and a variety of different populations are outlined. Changes in hypermobility across the lifespan, including differences between adults and children are explored. The psychological and psychosocial impact of JHS/EDS-HT is evaluated. Lastly, treatment strategies for JHS/EDS-HT are outlined and compared to other conditions.

1.3.2 Chapter Three: Research Methods & Methodology

This chapter outlines a summary of the methods used to conduct this research, including consideration of the research paradigms underpinning the research, an

overview of pragmatism and the choice to use mixed methods for the research design. Consideration is given to rigour in qualitative research, including how the researcher's dual position as an 'insider/outsider' with EDS-HT was considered and managed by design. The importance of networking and assistance from patient support groups and the researcher's partnership with a Patient Research Partner (PRP) were explored. Conclusively, theories relating to the psychosocial, cognitive and behavioural impact of JHS/EDS-HT were evaluated.

1.3.3 Chapter Four: Study 1: The lived experience of Joint Hypermobility and Ehlers-Danlos Syndromes: A systematic review and thematic synthesis.

This chapter presents a systematic review of all published qualitative data relating to men's and women's lived experiences of JHS/EDS. The choice to focus on EDS, rather than EDS-HT was due to the lack of distinction between patients with EDS-HT, and those with other subtypes of EDS within the qualitative data. It was not clear whether quotes were from participants who had the hypermobility subtype, or other subtypes of EDS. For this reason, those with all EDS subtypes were included for analysis. This chapter recognised that while people with JHS and EDS may experience significant anxiety, depression and psychological distress (as outlined in Chapter 2), there has yet to be a comprehensive systematic review examining the data produced by participants themselves. Therefore, this review provided a novel focus and insight into these experiences.

1.3.4 Chapter Five: Study 2: Exploring the psychosocial impact of Joint Hypermobility and Ehlers-Danlos Syndrome in adult men and women.

Recognising that there was still scope for a more detailed exploration of the psychosocial impact of JHS/EDS-HT, as well as the barriers and facilitators to coping and self-management, this study used semi-structured telephone interviews with participants purposively sampled to better represent ages, gender and ethnicities across the UK. Questions posed to participants were drawn from the results of the systematic review and thematic synthesis reported in Chapter 4. The resulting

themes, facilitators, and barriers identified during these interviews were carried across to Study 3 in Chapter 6.

1.3.5 Chapter Six: Study 3: Developing a self-management intervention to manage JHS and EDS-HT using behaviour change theory.

This third study of the research triangulated the findings from Study 1 and 2, mapping this data onto a theoretically driven method of behaviour change; The Behaviour Change Wheel (BCW), comprised of The Theoretical Domains Framework (TDF) and capability, opportunity, motivation-behaviour (COM-B) models (Michie *et al.*, 2005b). This chapter discusses and illustrates the multilevel refinement of the identified behaviour change interventions. These interventions were presented to two focus groups of stakeholders with JHS/EDS-HT from across the UK. Participants discussed, appraised, ranked and voted for their preferred self-management interventions using a Modified Nominal Group Technique consensus method. Options for preferred content and ideas for future research are explored.

1.3.6 Chapter Seven: Discussion

This chapter gives an overview of the results, and how these can be related to the wider literature. Results from each chapter of the thesis are considered, including the strengths and limitations of the work. Proposed ideas and recommendations for future research are discussed. Conclusions in relation to the overall aims are made.

2 Chapter 2: Background

This background chapter focuses in greater detail on JHS and EDS-HT, including definitions, the history of each condition and diagnostic criteria. Updates to the diagnostic criteria and nosology in 2017 are outlined and critically evaluated. The chapter explores epidemiology and differences in rates of hypermobility in terms of age, ethnicity and gender. The literature relating to the psychosocial impact of JHS/EDS-HT in terms of anxiety, depression and quality of life is discussed. Finally, current treatment options for JHS/EDS-HT within primary care are considered, and limitations of the current literature evaluated.

2.1 How is Ehlers-Danlos Syndrome defined and diagnosed?

This section will examine the various subtypes of EDS, highlighting typical methods used in identification, classification and diagnosis. Various debates and controversies surrounding the diagnosis will also be examined, including evidence of similarities and diagnostic overlaps between EDS-HT and JHS.

While references to people with easy bruising, lax joints and multiple scars can be traced as far back as 400BC (Parapia and Jackson, 2008), many early, anecdotal accounts of EDS feature patients using their unusual hypermobility skills to their advantage as circus exhibitionists or contortionists (Murray and Tyars, 1940, Grahame and Beighton, 1969). In 1901, dermatologist Edvard Ehlers presented the case of a patient with a history of loose joints, frequent knee subluxations and easily bruised, hyperextensible skin to the Dermatological Society of Denmark (Parapia and Jackson, 2008), calling the syndrome *'cutis laxa'*, or 'loose skin' (Royce and Steinmann, 2003). Seven years later in 1908, a French dermatologist, Henri-Alexandre Danlos described a second similar patient with loose, hypermobile joints, thin, hyperextensible skin and "mollusciod pseudotumors"; nodules under the surface of the skin, caused by chronic herniation of subcutaneous fatty tissues (Maltz *et al.*, 2001, Parapia and Jackson, 2008). Frederick Parkes Weber, a London

dermatologist, was the first to give the diagnosis '*Ehlers-Danlos syndrome*' to patients displaying the symptom triad of hyperextensible skin, hypermobile joints and fragility of the skin and blood vessels (Weber, 1936).

Classification of EDS began in the 1960s, with organisation of three (Barabas, 1967), five (Beighton, 1968) and seven (Mccusick, 1972) subtypes of EDS. By 1988, the International Nosology of Heritable Disorders of Connective Tissue, or the 'Berlin Nosology', formally identified eleven EDS subtypes using Roman numerals (Type I, Type III, Type VI etc.). Diagnosis was based on inheritance patterns and clinical findings (Beighton, 1988, Malfait *et al.*, 2017).

However, due to considerable diagnostic confusion regarding symptom overlap between subtypes of EDS, and subsequent advances in the understanding of underlying genetic influences, the nomenclature was updated in 1998 to the 'Villefranche Nosology' (Abel and Carrasco, 2006, Beighton *et al.*, 1998). With sponsorship from the Ehlers Danlos National Foundation (USA) and Ehlers Danlos Support Group (UK), in 1997 a team of geneticists met at Villefranche-Sur-Mer, France in an effort to bring coherence to the variety of both common and rare subtypes of EDS. The Villefranche Criteria identified subtypes primarily on the underlying genetic cause of each type. While some merely changed names to give a greater indication of the diagnostic appearance (e.g. EDS Type III became Hypermobility type), others merged to create six new major EDS subtypes (See Table 2.1; (Beighton *et al.*, 1998).

Major diagnostic criteria were chosen due to their infrequency in both other conditions and in the general population, making these symptoms highly suggestive of EDS. For example, for the Classical subtype of EDS, the major diagnostic criteria were skin hyperextensibility, widened atrophic scars and joint hypermobility, whereas the Hypermobile subtype of EDS featured the major diagnostic criteria of hyperextensible and/or smooth, velvety skin, in addition to generalised joint hypermobility (Castori, 2012). Minor diagnostic criteria could contribute to a diagnosis, but were not as suggestive, such as hernias, easy bruising, or musculoskeletal pain. For example, for the Classical subtype of EDS, minor diagnostic criteria included mulluscoid pseudotumors, muscle hypotonia or motor delay in infancy, or easy bruising. For EDS-HT, minor diagnostic criteria included recurring

joint dislocations and chronic joint or limb pain (Castori, 2012). Other, rare types of EDS included genetic variations and alterations appearing in single families only (Beighton *et al.*, 1998).

Table 2.1 Villefranche Criteria; Beighton *et al.,* (1998).

1) **Classical type**; Characterised by skin hyperextensibility, wide atrophic scars (manifestation of tissue fragility) and joint hypermobility. Caused by a defect in collagen type V.
2) **Hypermobility type**; Features stretchy and/or velvety smooth skin and generalised joint hypermobility.
3) **Vascular type**; Thin, translucent skin, arterial, intestinal or uterine fragility or rupture. Extensive bruising and a characteristic facial appearance (thin lips, 'pinched' nose, prominent eyes). Caused by structural defects in type III collagen.
4) **Kyphoscoliosis type**; Severe muscle hypotonia at birth, progressive scoliosis at birth, generalised joint hypermobility, scleral fragility, rupture of the ocular globe. Due to a deficit in collagen modifying enzyme.
5) **Athrochalasia type**; Severe, generalised joint hypermobility with recurrent subluxations. Congenital bilateral hip dislocation. Caused by mutations leading to deficient processing of Type I collagen.
6) **Dermatosparaxis type**; Severe skin fragility. Sagging, redundant skin. Due to deficiency of procollagen I N-terminal peptidase caused by allele mutation.

2.2 Overlapping conditions and the need for new criteria: JHS and EDS-HT

By far the most pressing debate surrounding the diagnosis of EDS concerned whether the Hypermobile form of EDS (EDS-HT) was the same condition as Joint Hypermobility Syndrome (JHS), formerly known by a variety of labels such as Benign Joint Hypermobility or Familial Joint Hypermobility Syndrome. Due to the severe pain experienced by some patients, the reference to the disorder as 'benign' has fallen out of favour (Grahame, 2001, Tofts *et al.*, 2009).

Rheumatologists Kirk, Ansell and Bywaters at Hammersmith Hospital in London were the first to reference the term 'Hypermobility Syndrome' in 1967; defined as joint hypermobility associated with musculoskeletal pain in otherwise healthy participants. While the authors recognised the existence of Ehlers-Danlos Syndrome, Kirk and colleagues suggested that if patients did not show signs of hyperextensible skin, a high palate or easy bruising then they instead suffered from Hypermobility Syndrome, rather than true Ehlers-Danlos syndrome (Kirk *et al.*, 1967).

The same year in Lambeth, Peter Beighton published a study of 100 patients from southern England with EDS, which at the time had only been divided into three broad EDS subtypes (Barabas, 1967). Beighton remarked that EDS patients could also have very mild hypermobility, varying evidence of elasticity or easy bruising and some having no skin manifestations at all (Beighton, 1968). With this in mind, it seems doubtful that patients in Beighton's (1968) study, if examined under Kirk, Ansell and Bywaters' (1967) criteria, would have consistently met the conditions for a diagnosis of EDS.

Certainly, many clinicians trying to differentiate between JHS and EDS-HT found it very difficult to tell the two apart. Bird, Tribe and Bacon, in a 1978 study of patients with JHS, encountered challenges when identifying which patients to exclude as having the hypermobility type of EDS (EDS-HT). They suggested that, regardless of the genetic inheritance, JHS may be part of "*a generalised connective tissue disorder that involves all parts of the body*" (Bird *et al.*, 1978), p. 210).

Both JHS and EDS-HT continued to run parallel to each other over several decades, despite yet more symptomatic similarities between the two conditions being identified (Grahame, 2013). These included anxiety disorders and phobias (JHS: (Bulbena *et al.*, 1988); EDS-HT: (Lumley *et al.*, 1994), problems with chronic joint and muscle pain (JHS: (Kirk *et al.*, 1967), EDS-HT: (Sacheti *et al.*, 1997) and gastrointestinal issues (JHS: (Fikree *et al.*, 2014), EDS-HT: (Beighton *et al.*, 1969). Links to Postural Tachycardia Syndrome (POTS), were also demonstrated in EDS (Wallman *et al.*, 2014) and JHS (Gazit *et al.*, 2003, Kanjwal *et al.*, 2011). POTS is thought to be due in part to increased blood vessel laxity, causing blood to pool in the legs and feet (Wallman *et al.*, 2014). Patients experience large jumps in heart

rate (>40bpm) when changing position, leading to symptoms of palpitations, fatigue, dizziness and fainting (Kanjwal *et al.*, 2011).

In 1998 the diagnostic criteria for JHS and EDS-HT overlapped considerably (see Table 2.2 below), with similar Beighton Score requirements, recurrent joint pain and dislocations.

Table 2.2: Comparisons between the revised (1998) Brighton Criteria (Grahame, 2001) and Villefranche Criteria (Beighton *et al.,* 1998).

Brighton Criteria (JHS)	Villefranche Criteria (EDS-HT)
Major criteria: • Beighton score >4/9 • Joint pain for >3 months in >4 joints	**Major criteria:** • Beighton score >5/9 • Hyperextensible and/or smooth, velvety skin
Minor Criteria: • History of joint dislocations • Pain in 1-3 joints • Hyperextensible skin with stretch marks or scarring • Marfan-like appearance • History of varicose veins, hernias and visceral prolapses • Eye signs, eyelid laxity	**Minor Criteria:** • Recurring joint dislocations • Chronic joint/limb pain • Positive family history

Despite some claims that the key to differentiating between the two syndromes lay in skin manifestations, (with hyperextensible skin more likely to result in a diagnosis of EDS-HT than JHS; (Tofts *et al.*, 2009) as we have seen in aforementioned studies this is not always the case (Beighton, 1968). Beighton also noted in the Villefranche criteria that skin manifestations in the hypermobile type may vary considerably (Beighton *et al.*, 1998). In addition, considerable difficulties replicating and measuring variances in skin extensibility and estimated smoothness between JHS and EDS participants in a standardised experimental setting have been

reported (Remvig *et al.*, 2009). As it was possible to distinguish JHS and EDS-HT from other heritable disorders of connective tissue, but not from each other, leading specialists proposed that EDS-HT and JHS were one and the same condition, and recommended the need for a more appropriate label for this group of patients (Tinkle *et al.*, 2009, Castori, 2012).

2.3 Changes to the diagnostic criteria: Hypermobility Spectrum Disorder (HSD) and Hypermobile Ehlers-Danlos Syndrome (hEDS)

In 2017, the classification of Joint Hypermobility Syndrome and Ehlers-Danlos syndrome was updated (Malfait *et al.*, 2017). Since the publication of the original Villefranche criteria in 1998, a greater variety of EDS subtypes, and the associated genetic mutations responsible, had been identified. A revised International EDS Classification was proposed, which recognised thirteen different subtypes of EDS (see Table 2.3). For each subtype, a new set of clinical diagnostic criteria was suggested (Malfait *et al.*, 2017).

As with the prior 1997 Villefranche classification, each EDS subtype is associated with major and minor diagnostic criteria (Malfait *et al.*, 2017). These criteria were chosen due to their high diagnostic specificity. For example, a major criterion would be present in the vast majority of individuals with a certain subtype of EDS. Minor criteria would not have the same degree of diagnostic specificity, but the presence of such a characteristic would help to support the EDS diagnosis (Malfait *et al.*, 2017). In the case of hypermobile Ehlers-Danlos syndrome (hEDS), the genes responsible for this subtype are still yet to be identified, and therefore diagnosis of the subtype is still reliant on clinical findings and assessment (Castori *et al.*, 2017), which are outlined below.

Table 2.3: 2017 Clinical classification of the Ehlers-Danlos Syndromes, including inheritance pattern and genetic basis (if known. Adapted from Malfait *et al.,* 2017).

	Clinical EDS Subtype	Abbreviation	IP	Genetic basis	Protein
1.	Classical EDS	cEDS	AD	Major: COL5A1, COL5A1, Rare: COL1A1 c.934C>T, p.(Arg312Cys)	Type V collagen, type I collagen
2.	Classical-like EDS	clEDS	AR	TNXB	Tenascin XB
3.	Cardiac-valvular EDS	cvEDS	AR	*COL1A2* (biallelic mutations that lead to *COL1A2*NMD and absence of pro α2(I) collagen chains)	Type I collagen
4.	Vascular EDS	vEDS	AD	Major: COL3A1 Rare: COL1A1 c.934C>T, p.(Arg312Cys), c.1720C>T, p.(Arg574Cys), c.3227C>T, p.(Arg1039Cys),	Type III collagen
5.	Hypermobile EDS	hEDS	AD	Unknown	Unknown
6.	Arthrochalasia EDS	aEDS	AD	COL1A1, COL1A2	Type I collagen
7.	Dermatosparaxis EDS	dEDS	AR	ADAMTS2	ADAMTS-2
8.	Kyphoscoliotic EDS	kEDS	AR	PLOD1, FKBP14	FKBP22
9.	Brittle cornea syndrome	BCS	AR	ZNF469	ZNF469
10.	Spondylospastic EDS	spEDS	AR	B4GALT7, B3GALT6	β4GALT7 β3GALT6
11.	Musculocontractural EDS	mcEDS	AR	CHST14, DSE	D4ST1, DSE
12.	Myopathic EDS	mEDS	AD or AR	COL12A1	Type XII collagen
13.	Peridontal EDS	pEDS	AD	C1R, C1S	C1r, C1s

Definitions: IP: inheritance pattern; AD: autosomal dominant; AR: autosomal recessive; NMD: Nonsense-mediated mRNA decay.

2.4 The revised 2017 diagnostic criteria

As explained previously, while originally thought of as two separate disorders, the diagnostic criteria for EDS-HT and JHS had a great number of overlapping features (Beighton *et al.*, 1988, Grahame *et al.*, 2000). Since the publication of Tinkle and colleagues (2009) paper outlining the similarities between JHS and EDS-HT, these

were considered to be interchangeable terms (JHS/EDS-HT). This was further supported by work by Castori and colleagues (2014) in a segregation study, who found that members of the same family could match the diagnostic criteria for both JHS and EDS-HT (Castori *et al.*, 2014, Castori *et al.*, 2017). These findings emphasised the need for more robust diagnostic criteria that also took into account the wide spectrum of presentation, from mild but symptomatic generalised joint hypermobility, to individuals with more severe multi-systemic involvement (Tinkle *et al.*, 2017).

The 2017 diagnostic criteria for the hypermobility subtype of EDS proposed two new conditions; criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS, formerly known as Ehlers-Danlos Syndrome Type III and Ehlers-Danlos Syndrome, Hypermobility Type), and criteria for Hypermobility Spectrum Disorders (HSD), for persons who may not meet the stricter diagnostic criteria for hEDS, but still have clinically significant joint hypermobility (Tinkle *et al.*, 2017).

In this updated criteria, diagnosis of hEDS can be given to persons who meet all of the criteria illustrated below. Criteria were chosen to reduce heterogeneity, and improve efforts to identify the underlying genetic cause(s) of the hypermobile EDS subtype. It was hoped that by identifying the underlying genetic link, that diagnosis could be more straightforward, and therefore clinical management of hEDS may improve (Malfait *et al.*, 2017). The 2017 clinical diagnosis of hEDS requires symptoms present in each of the three criteria, that is, criteria one, two and three.

2.4.1 Criterion one: Generalised Joint Hypermobility (GJH)

This updated criterion features the same Beighton Score as in the 1998 criteria, described in the previous Thesis Overview Chapter, to assess GJH. While the original cut-off was a score of ≥5, the new criteria proposed a variety of cut-offs in order to meet the criteria of hEDS:

- ≥6 for pre-pubertal children and adolescents,
- ≥5 for pubertal men and women up to the age of fifty,
- ≥4 for those over fifty years of age.

These changes reflected the variations in joint range of motion (ROM) and laxity over the lifetime (Malfait *et al.*, 2017, Singh *et al.*, 2017), with pre-pubertal children and adolescents found to score higher when compared to adults and older people (Remvig *et al.*, 2007). These changes were made in an effort to reduce under-diagnosis of hEDS in older populations, and potentially over-diagnosis in children (Malfait *et al.*, 2017). The authors also indicated that if clinical examination of the joint is not possible, due to prior surgical intervention, joint degeneration, or limitations to range of movement, that in adults the assessment of GJH may be completed using the five point questionnaire (5PQ, see Table 2.4, (Hakim and Grahame, 2003), although this scale has yet to be validated in children. Therefore, should the Beighton Score be one point below the corresponding cut-off point, and the 5PQ is positive (two or more affirmative answers), then the person can be diagnosed with GJH (Malfait *et al.*, 2017).

2.4.2 Criterion two: two or more of Features A-C (for example, A and B; A and C; B and C; A, B and C):

Feature A: systemic manifestations of a more generalised connective tissue disorder (five must be present; (Malfait *et al.*, 2017):

1. Unusually soft or velvety skin.
2. Mild skin hyperextensibility.
3. Unexplained stretch marks, (such as on the back, groin, thighs, breast and/or abdomen) in adolescents, men, or pre-pubertal women who do not have a history of significant weight gain or loss.
4. Bilateral piezogenic papules of the heel (small spheres of fat that appear under the skin with pressure).
5. Recurrent or multiple abdominal hernia (e.g. umbilical, inguinal, crural).
6. Atrophic scarring involving at least two sites (without the formation of truly papyraceous and/or hemosideric scars as seen in classical EDS.

7. Pelvic floor, rectal, and/or uterine prolapse in children, men, or women who have not experienced pregnancy (without a history of morbid obesity or any other known predisposing medical condition).
8. Dental crowding and a high arched or narrow palate.
9. Anacrodactyly, as defined in one or more of the following: (I) positive wrist sign (Steinberg sign) on both sides; (ii) positive thumb sign (Walker sign) on both sides.
10. Arm span to height ratio ≥ 1.05.
11. Mitral valve prolapse (mild or greater).
12. Aortic root dilation with a Z-score more than +2.

Feature B: Positive family history, with one or more first-degree relatives independently meeting the 2017 diagnostic criteria for hEDS.

Feature C: Musculoskeletal complications (must have at least one)

1. Musculoskeletal pain in two or more limbs, recurring daily for at least three months.
2. Chronic widespread pain for ≥3 months.
3. Recurrent joint dislocations or frank joint instability, in the absence of trauma (A or B):
    a. Three or more non-traumatic dislocations in the same joint, or two or more non-traumatic dislocations in two different joints occurring at different times.
    b. Medical confirmation of joint instability at two or more sites not related to trauma.

2.4.3 Criterion 3: all the following prerequisites must be met:

1. Absence of unusual skin fragility, which should prompt consideration of other types of EDS.
2. Exclusion of other heritable and acquired connective tissue disorders, including autoimmune conditions. In patients with an acquired connective

tissue disorder (such as lupus or rheumatoid arthritis), additional diagnosis of hEDS requires meeting both features A and B of criterion two.

3. Exclusion of alternative diagnoses that may include joint hypermobility by means of hypotonia and/or connective tissue laxity (such as neuromuscular disorders), other HDCT's (Loeys-Dietz syndrome, Marfan syndrome), and skeletal dysplasias (such as Osteogenesis Imperfecta).

Additional comment by the authors (Malfait et al., 2017)

Although many other features are associated with hEDS, they are not currently sufficiently specific or sensitive to be included in the final diagnostic criteria. These include fatigue, postural orthostatic tachycardia syndrome (POTS), functional gastrointestinal disorders, anxiety, depression, and sleep disturbance. Although not part of the diagnostic criteria, the presence of these additional symptoms may prompt consideration of hEDS as a differential diagnosis.

2.5 Critical observations regarding the new 2017 criteria

The authors of the new diagnostic criteria admitted that as a genetic link for hEDS has yet to be identified, and compared to other subtypes of EDS there is no "gold standard" genetic test to support or refute a diagnosis of hEDS (Malfait *et al.*, 2017), it was anticipated that future research would lead to potential revisions and changes to the hEDS criteria over time.

Interestingly, despite fatigue being noted as having a significant impact on those with EDS, and severe fatigue disproportionately affecting those with JHS/EDS-HT (86%; (Voermans *et al.*, 2010) compared to those with other EDS subtypes, no consideration has been given to the measurement or impact of fatigue in the 2017 criteria (To *et al.*, 2019).

In addition, the revised criteria still uses the Beighton Score as a measure of hypermobility, which has received criticism from several authors. First to consider is the redundancy of the forward lumbar flexion element of the criteria in participants with trained flexibility, such as participants in dance, gymnastics, yoga or Pilates. Due to the coached nature of the movement in professional ballet dancers (Gannon and

Bird, 1999, Klemp and Learmonth, 1984), all 82 participants in Chan and colleagues (2018) study were able to place their palms flat on the floor with their knees fully extended. Secondly, the Beighton Score only measures a set few joints (the lumbar spine, hips, elbows, knees, wrists, thumbs and fifth metacarpophalangeal joints, each in a singular sagittal direction of movement (Chan *et al.*, 2018). Despite the shoulders, neck, wrists, fingers and knees being indicated as the most frequently affected painful joints in EDS-HT (Voermans *et al.*, 2010), the Beighton score does not measure hypermobility of the neck, shoulder or ankle. Yet, in a sample of 2901 adolescents with a Beighton score of ≥6/9, 9.5% reported shoulder pain, 8.9% reported upper back pain, 8.6% neck pain and 6.8% ankle or foot pain (Tobias *et al.*, 2013). Similarly, in a sample of 615 adults with JHS who were asked about pain in the last week, 90% reported back pain, 84% shoulder pain, 80% neck pain, 66% ankle pain and 72% pain in their feet (Palmer *et al.*, 2017). A recent study has compared participants' Beighton Score and laxity of the shoulder joint using the Instability Severity Index Score (Whitehead *et al.*, 2018), finding that a participant's Beighton Score was a poor predictor of abnormal shoulder laxity, with low sensitivity (range= 0.40 – 0.48) and low positive predictive values (range= 0.13-0.31). Increasing the positive Beighton Score to ≥6 resulted in only a minimal improvement in the positive predictive values, indicating a need for clinicians to be cautious when relying on the Beighton Score alone (Whitehead *et al.*, 2018).

While still a reliable measure of joint hypermobility (Castori *et al.*, 2017), the validity of the Beighton Score in measuring clinically significant hypermobility has been brought into question (Nicholson and Chan, 2018). Future changes to the diagnostic criteria may wish to explore broader options for the assessment of hypermobility, using validated tools that cover a greater number of joints. One example is Lower Limb Assessment Scale (LLAS, (Ferrari *et al.*, 2005), which has been found to differentiate more effectively between lower limb hypermobility in adults (Chan *et al.*, 2018) and children (Ferrari *et al.*, 2005), when compared to the Beighton Score. The LLAS measures mobility in 12 bilateral tests of the hip, knee, ankle, tibiofibular and foot joints, with a unilateral cutoff score of ≥7/12 points, in both adults and children (Ferrari *et al.*, 2005, Meyer *et al.*, 2017). By measuring joint mobility at a multitude of joints, rather than the seven areas measured by the

Beighton Score, the test gives a more accurate indication of the extent of widespread hypermobility, and reduces the potential risk for the Beighton Score identification of 'false positive' hypermobility for those with laxity in only a few joints.

As noted previously, the Beighton Score only measures movement of joints in one sagittal movement plane. The Lower Limb Assessment Scale (LLAS) and Upper Limb Hypermobility Assessment Tool (ULHAT) measure joints in all 3 planes of motion (Ferrari *et al.*, 2005, Meyer *et al.*, 2017, Nicholson and Chan, 2018). The ULHAT measure has been tested on participants aged 18-40 years with varying degrees of upper limb hypermobility; known hypermobile participants (participants with medically confirmed JHS/EDS-HT), likely hypermobile participants (pre-professional and professional elite dancers) and a group of control participants from the University of Sydney (students and staff with no long-term training in activities likely to affect flexibility such as dance, yoga, Pilates or gymnastics (Nicholson and Chan, 2018). The ULHAT has been designed as a complimentary 12-question test to the 12 tests of the LLAS. Results indicated highly accurate results when identifying generalised joint hypermobility (with a cutoff score of ≥7/12), compared to clinical opinion. However, this pattern was not found when comparing identification of hypermobility using the Beighton score, which was found to significantly overestimate the prevalence of generalised joint hypermobility in controls, even when the cutoff was increased to ≥5/9, as in the 2017 criteria for pubertal men and women up to the age of fifty (Meyer *et al.*, 2017). The authors concluded that this discrepancy was likely due to discrepancies in what the Beighton score is measuring compared to the ULHAT, and recommend using the Beighton score as a preliminary screening measure for GJH, then using the ULHAT as a more refined secondary measure to examine the degree of joint hypermobility (Meyer *et al.*, 2017).

Although updated and refined to better identify participants with more severe manifestations of hEDS, the choice to continue to use the Beighton Score is still a significant limitation of the diagnostic criteria. It is likely that future diagnostic criteria will be refined to more accurately reflect GJH across the whole upper and lower limb spectrum of joints, rather than the limited joints assessed at present.

2.6 Prevalence of generalised joint hypermobility (GJH)

2.6.1 Prevalence in adults

2.6.1.1 Studies using the Five-Part Questionnaire (5PQ)

Some large population prevalence studies have used different methods to measure the prevalence of hypermobility remotely using a five item survey; the Five-Part Questionnaire (5PQ, see Table 2.4, (Hakim and Grahame, 2003). The questions are designed to indicate evidence of characteristics suggestive of GJH in the participant's lifetime. An affirmative score is one point, and a score of two or greater on the 5PQ has been reported to have a sensitivity of 80-85% and specificity of 80-90% when compared to a score of ≥4 on the Beighton score (Hakim and Grahame, 2003).

Table 2.4: The five-part questionnaire for identifying joint hypermobility (Hakim & Grahame, 2003).

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

Hakim and colleagues screened 483 monozygotic and 472 dizygotic female twins (age range 21-81 years) recruited from the UK St Thomas' Adult Twin Registry. Results indicated that GJH was present in 19.5% of monozygotic twins and 22.1% of dizygotic twins (Hakim *et al.*, 2004). A recent large-scale cross-sectional population survey in Aberdeen and Cheshire examined the population prevalence of joint hypermobility in adults ≥25 years using the 5PQ (Mulvey *et al.*, 2013). In this sample, 18% were classified as being hypermobile (Mulvey *et al.*, 2013).

2.6.1.2 Studies using the Beighton Score

Other studies have used the Beighton score to measure the prevalence of GJH, however the prevalence of GJH in the general population is difficult to establish, as studies typically focus on opportunity samples of participants recruited from specific populations. Studies of healthy volunteers reported a GJH prevalence of 17.6% in a sample of UK adults (n= 250, 151 UK women, median age 39 years, Beighton score ≥4/9, (Farmer *et al.*, 2010) and 21.1% in a sample of Spanish adults (n= 158, median, 64 women, age 31.9 years, Beighton score ≥4/9, (Bulbena *et al.*, 2011).

The prevalence of GJH differs between populations, with prevalence rates varying between no discernable joint hypermobility in an epidemiological survey in New Zealand (Klemp *et al.*, 2002), to 57% in a sample of Nigerian women (Beighton score ≥4/9,(Birrell *et al.*, 1994). Results have indicated Asian and African populations to have greater hypermobility prevalence compared to Caucasians (Beighton *et al.*, 1999), and percentages in these studies are highly variable. For instance, similar prevalence results to European participants were reported by Al-Jarallah and colleagues (Al-Jarallah *et al.*, 2017), who found a GJH prevalence of 22.3%; (14.5% of women and 29.4% of men) in Kuwaiti undergraduates, (n=390, 186 women, age range 18-29, Beighton score ≥4/9). Verhoven *et al.,* (1999) found a higher GJH prevalence of 30.8% after examining 705 nulliparous women in Tanzania (age range 9-36, mean age 17±4 years, Beighton score ≥4/9, (Verhoeven *et al.*, 1999). Similarly, in their study of GJH prevalence in university students in Lublin, Poland, the highest incidence of GJH (Beighton scores ≥5/9), was found in Taiwanese students, with 29% having GJH (Szalewska *et al.*, 2014). A study of Iraqi university students (n=1774, age range 20-24 years) indicated a GJH prevalence of 38.5% of women and 25.4% of men (Beighton score ≥4/9,(Al-Rawi *et al.*, 1985). Kwon and colleagues (2013) examined 403 Korean women (Beighton score 4/9 or greater, age range 24-50), and found a GJH prevalence of 50% (Kwon *et al.*, 2013). The highest GJH prevalence as measured by the Beighton Score was found in a study of Nigerian men (35%) and women (57%, n=204, age range 6-66, Beighton score ≥4/9,(Birrell *et al.*, 1994).

Yet, difficulties have been noted within the literature regarding the ability to compare epidemiological results between studies. Firstly, due to the changes in

diagnostic criteria over time, Beighton scores of ≥3/9 (Beighton *et al.*, 1973), ≥4/9 (Al-Rawi *et al.*, 1985, Farmer *et al.*, 2010), or ≥5/9 (Szalewska *et al.*, 2014) had been indicated as a measure of hypermobility by different authors. As a result, it can be very difficult to compare prevalence results between different populations (Verhoeven *et al.*, 1999), a difficulty that was noted in the upgraded 2017 diagnostic criteria (Malfait *et al.*, 2017). Secondly, as the relatively small sample sizes do not make up a nationally representative sample, these prevalence results cannot be generalised to the wider populations.

2.6.2 Prevalence across the lifespan

Although adults are the prime focus of this dissertation, hypermobility can also be influenced by age, with qualitative studies indicating that adults with JHS/EDS-HT have had problems associated with joint laxity since childhood (Berglund *et al.*, 2000, Palmer *et al.*, 2016b). Children generally tend to be more hypermobile than adults; with rates of GJH varying between 54.1% in preschool children (aged 5-6) from Parana, Brazil (Neves *et al.*, 2013) to 6.7% in schoolchildren from Kent (Carter and Wilkinson, 1964). In an evaluation of 6022 teenagers (average age 13.8 years, Beighton score ≥4/9) a GJH prevalence of 27.5% for girls and 10.6% for boys (Clinch *et al.*, 2011) is comparable to GJH prevalence in a sample of 861 students (mean age 15.4+/-1.1 years), with GJH prevalence of 16.2% for girls and 7.2% for boys (Seckin *et al.*, 2005). Pre-pubescent boys in some studies have been shown to have a similar (Ruperto *et al.*, 2004) or in one case a higher prevalence of GJH (73%, n=26) compared to girls (29% n=48, (Carter and Wilkinson, 1964).

Research has indicated that GJH declines naturally as children reach puberty, but the rate at which this occurs has yet to be confirmed as results vary between declines in GJH aged 9-12 in girls, followed by an increase in GJH at the age of 15 (Jansson *et al.*, 2004). Other research has found highest GJH at birth, with rapid declines throughout childhood, moderate declines in adolescence and reduced declines in GJH during adulthood (Beighton *et al.*, 1999).

In adults with GJH, laxity also progressively decreases over time with increasing age (Jaffe *et al.*, 1988, Kwon *et al.*, 2013, Larsson *et al.*, 1993) and measures of hypermobility are designed take this into account. For example, the

5PQ asks questions prefaced by “can you now, (or could you ever)?” to reflect the decreasing levels of joint laxity in adulthood compared to childhood (Hakim and Grahame, 2003).

2.6.3 Gender differences in GJH

As we have seen in the prevalence results explored previously, women are more likely to have GJH than men (Hakim *et al.*, 2004, Remvig *et al.*, 2007, Seow *et al.*, 1999, Simmonds and Keer, 2007). Although consideration has been given to the gender differences seen in GJH and JHS/EDS-HT as being due to hormonal differences, research has yet to investigate any potential hormonal difference in men and women with JHS/EDS-HT. A link observed between increased joint laxity in healthy women without JHS/EDS-HT during pregnancy has given some credibility to the idea that hormones might play a part in joint laxity (Marnach *et al.*, 2003). However, it is noted that while relaxin, cortisol, estradiol and progesterone levels are raised during pregnancy, this theory does not account for high rates of hypermobility in young children (Marnach *et al.*, 2003).

2.6.4 Prevalence of JHS/EDS-HT in adult populations

Although the epidemiology of EDS-HT and JHS has yet to be studied, the prevalence of EDS has been estimated at between 1 in 5000 (Steinmann *et al.*, 2003). For the 2017 reclassification, the prevalence of hEDS as the most common EDS subtype was thought to be liable to encompass 80-90% of all EDS cases. The authors therefore proposed that the prevalence of hEDS was presumed to be at least 1 in 5000 (Tinkle *et al.*, 2017). While the true incidence in the UK population has yet to be determined, reported incidences have indicated that 30% of patients referred to a musculoskeletal triage clinic in London (Connelly, 2015); 39% of attendees to a pain clinic (To *et al.*, 2019) and between 37% and 45% of patients referred to a London Rheumatology clinic met the diagnostic criteria for JHS (Grahame and Hakim, 2006).

2.7 The impact of JHS/EDS-HT

This section provides an overview of the literature pertinent to the physical and psychosocial impact of joint hypermobility. Because this research was published prior to the 2017 criteria, the terms JHS and EDS-HT are used throughout. As JHS and EDS-HT were considered the same condition, research relating to both syndromes has been included and indicated accordingly.

2.8 Chronic pain and quality of life

Both EDS-HT and JHS have been associated with severe chronic pain.
While it is not clear why some people with JHS/EDS-HT develop chronic pain and others do not (Engelbert *et al.*, 2017), chronic pain in JHS/EDS-HT is thought to be due to repeated micro-trauma, caused by biomechanical loading of the joints and muscles at the very end of their range of motion (Booshanam *et al.*, 2011). This biomechanical load, in combination with poor postural control, poor awareness of joints in space (proprioception) and decreased muscle strength may also make the joints more susceptible to injury (Ferrell *et al.*, 2007, Rombaut *et al.*, 2012, Scheper *et al.*, 2013). Indeed, a study of gait and knee joint loadings in people with GJH (Beighton score ≥4) indicated increased knee joint loadings and joint movements during walking, which may give an explanation for the increased rate of osteoarthritis in the JHS/EDS-HT population (Simonsen *et al.*, 2012). Furthermore, research has indicated that those with hypermobility may have an increased sensitivity to pain, termed hyperalgesia. In measuring pressure thresholds in symptomatic and asymptomatic areas, those with JHS/EDS-HT had significantly lower pressure pain thresholds, indicating a generalised hyperalgesia (Rombaut *et al.*, 2015). Later work by Scheper and colleagues (2017) confirmed generalised hyperalgesia in both adults and children with JHS/EDS-HT, and found hyperalgesia to be discriminative between healthy controls, those with GJH and participants with JHS/EDS-HT (Scheper *et al.*, 2017).

Chronic pain can have notable effects on patients' activities of daily living, and health-related quality of life. In a Danish study of participants from the Dutch EDS Foundation support group, severe chronic pain was a common finding associated with moderate to severe impairment in daily functioning (Voermans *et*

al., 2010). Of all EDS subtypes, pain was most predominant and severe in those with the hypermobile type of EDS, with the shoulders, neck, wrists, fingers and knees indicated as the most frequently affected joints (Voermans *et al.*, 2010). Similarly, Ross and Grahame (2011) reported that of 700 patients with JHS attending London's University College Hospital (UCH) Hypermobility Clinic, 168 (24%) reported significant pain, disability and a poor quality of life. Pain was regularly associated with a progressive loss of movement due to fear of pain (kinesiophobia), and was described as being largely unresponsive to analgesics (Ross and Grahame, 2011). An investigation into shoulder function, pain and health-related quality of life indicated that those with JHS/EDS-HT had lower shoulder functioning, generalised pain (96.2% JHS/EDS-HT vs 20.7% controls) and lower health-related quality of life as measured by the SF-36 Physical Component, compared to controls (Johannessen *et al.*, 2016).

Hypermobility-related chronic pain has been cited as plunging patients into a "*vicious downward spiral*" (Grahame, 2009), p. 430) or "*domino effect*" of deteriorating function (Simmonds and Keer, 2007), p. 6). This can lead to reduction in daily activities due to pain, kinesiophobia, fear of re-injury, and decreasing self-confidence, self-efficacy and independence (Grahame, 2009).

2.9 Relationship between JHS/EDS-HT and osteoarthritis (OA)

Although GJL has historically been associated as a risk factor for OA (Bridges *et al.*, 1992, Grahame, 1989), these results have been variable, and the true relationship between GJL and OA remains unknown.

Recent research has not found an association between GJL and multiple-joint osteoarthritis (MJOA). Gullo and colleagues (2019) cross-sectional study examined 1677 participants (68% women, mean age 69 years) with GJL (Beighton score ≥4) and used logistic regression to estimate odds ratios between GJL and MJOA. Of those examined, 4% had a Beighton score ≥4, and 63% met the definition of MJOA. Interestingly, GJL was associated with significantly lower odds of radiographic and symptomatic MJOA-1 (the first of three definitions of MJOA). Having GJL was associated with 78% lower odds of MJOA-1 (involving ≥1 interphalangeal nodes) and 58% lower (MJOA-1 at ≥2 sites of hip, knee and spine). There was no significant association between GJL and other definitions of MJOA (Gullo *et al.*, 2019). The

researchers concluded that overall, there was no positive association between GJL and MJOA (Gullo *et al.*, 2019).

In a large cross-sectional study of participants from the Carolinas region (mixed African American and Native American ancestry) and participants from cohorts in the US and UK were assessed for GJL (Beighton score ≥4), in addition to hand, knee and hip radiographs (Chen *et al.*, 2008). Using logistic regression, GJL was also noted to be associated with a decreased likelihood ratio of hand OA, which remained significant after adjustment for age or BMI. Furthermore, compared to those without GJL, participants with GJL had significantly fewer proximal interphalangeal (PIP) joints affected with OA ($P < 0.005$) and GJL was associated with a lower likelihood ratio of knee OA ($P = 0.02$).

An examination of fifty consecutive women referred to a rheumatologist with clinical hand OA, Jónsson et al., (1996) found that 31 of the 50 had a Beighton score ≥2, and 17 of the 30 had a Beighton score ≥4. Those with GJL had lower incidence of joint OA, both clinically and radiologically, with the participant's Beighton score correlating inversely with the number of joints affected by OA, both clinically (r_s -.053, $p < 0.001$) and radiologically (r_s -.041, $p < 0.01$). However, of those with severe first interphalangeal joint disease (CMC1), GJH (Beighton score ≥2) was present in 18 of 21 patients. The authors hypothesised whether, as opposed to systemic OA seen in the control population, the CMC1 joint OA seen in patients with GJL could be due to cartilage damage associated with ligament laxity (Jonsson *et al.*, 1996).

Bridges, Smith and Reid (1992) evaluated 130 consecutive patients referred for ergotherapy treatment in Iceland, of which 20 (15%) met the criteria for GJL (Beighton score ≥5). Of the 20, 12 (60%) had OA, compared to 33/100 (30%) of those without GJH. Although this is a significant difference ($P < 0.01$), due to the small sample size of patients with GJL (n = 20, all women) it is difficult to draw direct conclusions between GJH and OA (Bridges *et al.*, 1992).

Dolan and colleagues (2003) Chingford Study assessed 716 women (mean age 61 years), and found 79 (11%) had a Beighton score of >1, with only 1 participant having a Beighton score ≥4, indicating GJL (Dolan *et al.*, 2003). The Contompasis Scoring System was used to assess GJL, with scores >18 indicating GJL (McNerney & Johnston, 1979). Of the sample, 82 (11%) had a Contompasis score >22 and showed a reduced risk of knee OA (OR 0.48, 95% CI 027-083), but no significant difference was found in rates of hand or spine OA (Dolan *et al.*, 2003).

A potential protective mechanism between GJH and later development of OA was also noted by Kraus et al. Participants with a Beighton score ≥4 were found to have decreased likelihood of developing OA in their PIP joints, and similar results were also observed for those with a Beighton score ≥2 (Kraus *et al.*, 2004).

Due to the large variability between definitions of GJL between the studies, with Beighton scores of >1 (Dolan *et al.*, 2003) ≥2 (Jonsson *et al.*, 1996), ≥4 (Gullo *et al.*, 2019, Kraus *et al.*, 2004) or ≥5 (Bridges *et al.*, 1992) comparing and contrasting the findings between studies is difficult. It is clear from these results that future longitudinal research is required to truly establish the association between GJL, JHS/EDS-HT and OA. However, the suggestion by more recent findings that GJL may offer a protective mechanism against developing OA is an interesting consideration.

2.10 Fatigue in JHS/EDS-HT

Widespread pain and decreased muscle strength may also result in those with JHS/EDS-HT being more susceptible to fatigue (Castori, 2012). Severe fatigue, present in 84% of those with EDS-HT surveyed by Voermans and colleagues (2010) was also linked with severe pain. For 40% of the overall sample surveyed (made up of participants with all EDS subtypes), severe fatigue had a greater impact on their daily functioning than pain. Five possible determinants of fatigue were measured in the study, including: 1) sleep disturbances, 2) pain, 3) concentration problems, 4) social interaction, and 5) self-efficacy concerning fatigue (Voermans *et al.*, 2010).

However, these results were not broken down into EDS subtypes, but measured as a cross-section across all subtypes of EDS, making causal relationships between fatigue and JHS/EDS-HT difficult to quantify and compare (Voermans *et al.*, 2010). Participants with JHS/EDS-HT also perceived greater fatigue compared to a control group in a recent study of electrical stimulation of the musculocutaneous nerve and transcranial magnetic stimulation of the motor cortex (To *et al.*, 2019). This effect was thought to be due to altered central nervous system drive leading to 'central fatigue' (To *et al.*, 2019). Although the causes of fatigue in JHS/EDS-HT have not been investigated in detail to date, central fatigue may be due to higher effort required by the central nervous system to monitor imprecise physical movements, which might also link to poor proprioception and clumsiness seen in children (Fatoye *et al.*, 2008) and adults with JHS/EDS-HT (Camerota *et al.*, 2015, Smith *et al.*, 2014b, To *et al.*, 2019). Despite fatigue being a recognised symptom within JHS/EDS-HT, measures of fatigue do not feature in the revised 2017 hEDS/HSD diagnostic criteria (Malfait *et al.*, 2017), but have been recognised in the Bristol Impact of Hypermobility (BIoH) questionnaire (Palmer *et al.*, 2017).

2.11 Associated systemic involvement

Due to the widespread predominance of collagen within the body, a number of conditions are also associated with JHS/EDS-HT. As was mentioned briefly in the first chapter, Postural Orthostatic Tachycardia Syndrome (POTS) is a common finding in JHS/EDS-HT (Gazit *et al.*, 2003). POTS is a form of autonomic nervous system deregulation associated with large increases in heart rate on sitting up or standing (≥30 beats per minute, or increase in heart rate to ≥120 beats per minute). Symptoms of POTS can include dizziness, palpitations, a fast heart rate, shaking, sweating, and feeling faint (Gazit *et al.*, 2003, Kanjwal *et al.*, 2011). In a tilt table study of 35 patients with JHS/EDS-HT, 48.6% of patients had postural tachycardia and 31.4% showed orthostatic intolerance (a drop in blood pressure, (Celletti *et al.*, 2017).

Although the exact mechanism for POTS is unknown, is has been hypothesised that that the laxity of connective tissues in JHS/EDS-HT may also affect the collagen and elastin supporting the vascular system, such as the type III collagen,

elastic tissue and smooth muscle cells found in the tunica media, the middle layer of all arteries and veins (Wallman *et al.*, 2014). It has been estimated that this potential structural compromise in the blood vessels may alter venous return throughout the body (Wallman *et al.*, 2014).

Similarly, JHS/EDS-HT has also been associated with functional gastrointestinal problems. In a screening of 21 patients with EDS-HT, these included gastrointestinal discomfort (85.7%), chronic gastritis (66.7%), gastroesophageal reflux (57.1%), IBS symptoms (33.3%) and abdominal hernia (4.8%;(Castori *et al.*, 2010). A similar study of 21 patients with JHS by Zarate and colleagues (2010) also indicated high rates of abdominal pain (81%), bloating and nausea (57%), gastro-osophogeal reflux (48%) and constipation (38%, (Zarate *et al.*, 2010). Gastro-oesophegal reflux disease ($p<0.0001$), functional constipation and IBS ($p=-0.007$) were found to have the most significant impact on quality of life, in survey of patients with all EDS subtypes (Zeitoun *et al.*, 2013). Although less common, uterine, vaginal (Norton *et al.*, 1995) and rectal prolapse (Marshman *et al.*, 1987) can also be associated with GJH and JHS/EDS-HT (Carley and Schaffer, 2000, Castori *et al.*, 2010). This susceptibility to prolapse is also thought to be due to the inherent differences in the structure of connective tissues, making patients' with EDS more likely to experience pelvic organ prolapse or urinary incontinence (Carley and Schaffer, 2000, Stoddard and Myers, 1968). In summary, it is clear that due to the high prevalence of collagen within the body, those with GJH and JHS/EDS-HT can evidently experience a wide range of systemic symptoms as a result of their JHS/EDS-HT, many of which can have a negative impact on their daily functioning, and their quality of life.

2.12 Defining "psychosocial"

It is clear from the literature that patients with JHS/EDS-HT score highly on a number of measures of psychological distress. Dealing with a chronic multifactorial health condition such as JHS/EDS-HT can result in a variety of physical, psychological and social consequences, including psychological distress, depression (Bulbena *et al.*, 1993), (Gurer *et al.*, 2010), anxiety (Bulbena *et al.*, 1993), (Martin-Santos *et al.*, 1998), and quality of life (Ross and Grahame, 2011, Johannessen *et al.*, 2016). Other

psychosocial consequences can include social stigma, lowered self-esteem, issues with work, social lives, relationships with friends and family and feelings of fear about the future (Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015).

Problems with psychosocial functioning can be defined as as '*functioning problems that involve both psychological and social problems that people experience in their daily lives, and are associated with the health condition*' (Cabello *et al.*, 2012). Psychosocial functioning can also refer to a person's ability to perform daily tasks and to interact with others and society in a mutually adequate manner (Lam *et al.*, 2011). In the present research, psychosocial functioning can be defined as:

"The effect of psychological, social and environmental factors on individuals' thoughts and behaviour, as associated with JHS/EDS-HT."

Bodily changes associated with JHS/EDS-HT associated with soft tissue laxity such as atrophic scarring and frequent injuries may also result in concerns and impact regarding body image and sexuality. In addition, although little research to date has explored this area, the impact of hernias, pelvic, bladder or rectal prolapse may affect participants' feelings of attractiveness and body integrity (Berglund *et al.*, 2000).

In studies where the effects of depression (Bulbena and Berrios, 1993, Bulbena *et al.*, 2011, Gurer *et al.*, 2010), anxiety (Bulbena and Berrios, 1993, Martin-Santos *et al.*, 1998), and fear (Bulbena *et al.*, 2006, Pailhez *et al.*, 2011) have been studied in a JHS and EDS-HT population, psychological factors have been considered in isolation, not in addition to any potentially contributory social or psychosocial factors. Possible psychosocial factors such as social anxiety have been investigated using quantitative self-report questionnaire methods only, including the Mini Social Phobia Inventory (Mini-SPIN), a three-item scale (Bulbena *et al.*, 2011, Baeza-Velasco *et al.*, 2011a). This reliance on quantitative data, while useful and objective, has not given participants a chance to explain the broad impact of JHS/EDS-HT on their psychosocial functioning; their own lived experiences of JHS/EDS-HT.

Numerous studies have highlighted the need to take into account both the biological and psychosocial impacts of illness on patients. Although this research will focus on adults, children with JHS/EDS-HT have been found to have lower than expected mean values on measures of self-esteem, behaviour and psychosocial functioning (Pacey *et al.*, 2013). A strong negative correlation was also found between pain intensity and quality of life in children with JHS/EDS-HT, compared to those without the condition, and negative correlations between pain intensity and school, emotional and physical functioning on quality of life domains (Fatoye *et al.*, 2012). Similarly, both children and adolescents (age range 8-15 years) with JHS/EDS-HT also had significantly poorer results on the Paediatric Quality of Life inventory 4.0, and experienced disabling levels of fatigue on the Multidimensional Fatigue Scale, compared to children without JHS/EDS-HT (Pacey *et al.*, 2015).

While few have examined these factors in JHS/EDS-HT, psychosocial factors have been identified and examined in the chronic pain literature. For example, Moses and colleagues (2005) examined the psychosocial challenges facing women who cope with systemic lupus erythematosus (SLE, often abbreviated to lupus). Like JHS/EDS-HT, lupus affects considerably more women (90%) than men (10%), and is also marked by significant fatigue, joint and muscle pain (Auerbach *et al.*, 2013, Moses *et al.*, 2005). Given the unpredictability and life-long chronic nature of the disorder, patients also experience high rates of anxiety, depression and significantly decreased health-related quality of life. Using the SLE Needs Questionnaire (SLEQ), Moses and colleagues found that patients with lupus (n= 386) reported numerous unmet psychosocial needs; 24% required sexual information, 39% needed help meeting the extra costs of their disease, 50% required assistance and support from others to cope with their condition and 64% needed assistance explaining their condition to others (Moses *et al.*, 2005). Auebach *et al.,* (2013) also found that frequent increases in symptoms, or lupus 'flares' resulted in the highest need for help with depression, anxiety and social challenges, such as having to modify career plans and availability of friends and social networks (Auerbach *et al.*, 2013). Given the similarities between JHS/EDS-HT and lupus, it may be that patients with JHS/EDS-HT will also require help and support in coping with their condition.

2.13 Psychosocial impact of JHS/EDS-HT

2.13.1 Emotional functioning

Although the association between chronic pain and psychological distress, particularly anxiety and depression, has been well documented for other chronic pain conditions, such as osteoarthritis, rheumatoid arthritis and lupus, little research has examined the psychosocial impact of JHS/EDS-HT. As the influence of psychological and psychosocial factors have the power to influence patients' experience of pain (Moore *et al.*, 2004) a greater understanding of how these affect participants' lives is vital, in order to ensure optimal self-management of their condition.

Chronic pain conditions such as JHS/EDS-HT can have a substantial impact on a person's psychological wellbeing. For example, patients with Fibromyalgia also reported more total psychological distress, and a lower quality of life (Verbunt *et al.*, 2008), while a nationally representative sample of patients in the United States found that those with arthritis were more than twice as likely to suffer anxiety and depressive symptoms compared to those without the condition (Shih *et al.*, 2006). Studies examining the psychosocial impact of JHS/EDS-HT in terms of emotional functioning are outlined below.

2.13.2 Anxiety

An important systematic review by (Smith *et al.*, 2014b) examined the relationship between GJH, JHS/EDS-HT and psychological distress in a meta-analysis. The review included both case-control and cohort studies, in order to assess the prevalence of psychological distress for people with JHS/EDS-HT. Participants were included if they had a clinical diagnosis of GJH, defined as a Beighton score ≥4, but were excluded if they had any other connective tissue disorder, such as other EDS subtypes or Marfan's Syndrome, with the exception of EDS-HT. Of the 172 articles identified, 14 met the inclusion criteria and were included for analysis (Smith *et al.*, 2014b). It is worth noting that due to the differences in diagnostic criteria over time, the diagnosis of JHS is quite variable between these studies, from a Beighton score ≥3 or ≥5 items of the Beighton's 'diagnostic scheme', (Bulbena *et al.*, 1993), Beighton

score ≥4 (Gurer *et al.*, 2010), Beighton score ≥5 (Martin-Santos *et al.*, 1998) which can make comparisons more difficult. The results of a meta-analysis of three studies (Bulbena *et al.*, 1993, Gurer *et al.*, 2010, Martin-Santos *et al.*, 1998) indicated that anxiety was four times more likely in participants with JHS compared to controls (OR 4.93, 95% CI 1.92, 10.4, *P* = 0.005; (Smith *et al.*, 2014b). The meta-analysis also indicated a statistically significant between-groups difference, with more severe anxiety symptoms in those with JHS compared to control participants (SMD= 0.53, 95% CI 0.31, 0.74, *P* <0.001) (Bulbena and Berrios, 1993, Bulbena *et al.*, 2004, Bulbena *et al.*, 2011, Baeza-Velasco *et al.*, 2011a, Ercolani *et al.*, 2008, Martin-Santos *et al.*, 1998).

Anxiety has been associated with JHS/EDS-HT in a number of studies. The first to make this association was Bulbena and colleagues (1993), who used a case-control design to test the association between JHS, anxiety and phobic disorders (agoraphobia, panic disorder, panic and agoraphobia, simple phobia) with patients recruited from the Hospital Del Mar, a teaching hospital serving a low-income area of Barcelona (Bulbena *et al.*, 1993). As mentioned previously, those with Beighton scores of ≥3, or scores of ≥5 items of the Beighton diagnostic scheme were classed as having JHS. This is quite a broad inclusion criteria, as most modern measures of GJH use a Beighton Score of ≥4. In addition, it is not clear what the 'Beighton diagnostic scheme' is in reference to, whether the authors are referring to the Beighton Score, or the Brighton Diagnostic criteria, as there is no citation given (Bulbena *et al.*, 1993). There was no significant difference between cases (n=114) and controls (n=59) in relation to the Hamilton Anxiety Scale (HAM-A), or for the prevalence of generalized anxiety disorder (10.5% JHS vs 5.1% controls, *P* = 0.269). However, statistically significant differences were found between cases and controls for agoraphobia (37.7% vs 11.9%), panic disorder (34.2% vs 6.8%), simple phobia (29.8% vs 8.5%), and for all combined psychiatric disorders (69.3% vs 22.0%,(Bulbena *et al.*, 1993).

A later investigation by Martin-Santos et al (1998) examined whether patients with panic disorder or agoraphobia (n=99) were more likely to suffer from JHS compared to two control groups of age- and sex-matched psychiatric patients (n=99) and medical patients without anxiety (n=64). The study also examined whether mitral valve prolapse modified or accounted for the situation (Martin-

Santos *et al.*, 1998). JHS was found in 67.7% of patients with an anxiety disorder, 10.1% of psychiatric controls and 12.5% of medical control participants. There was a slightly higher than average incidence of mitral valve prolapse (8%), compared to 3% in the general population and no patients in the psychiatric control group (Martin-Santos *et al.*, 1998). When the results of the psychiatric (n= 64) and medical control groups (n=64) were combined (N=163) patients with anxiety were over 16 times more likely to present with JHS compared to controls (odds ratio = 16.9, $p<0.001$) and had a mean Hamilton Anxiety Score of 23.4, compared to mean scores of 9.4 (psychiatric control group) and 2.9 (medical control group). Though, the direction of the results is unclear. For example, there is no evidence that panic leads to JHS, therefore the authors suggest that joint laxity may lead to a panic disorder (Martin-Santos *et al.*, 1998). Factors that may precipitate panic disorder in adulthood, such as early life stressors, lung disease and smoking (Breslau and Klein, 1999) were not considered in the study. In addition, whereas all participants were newly diagnosed and clinically representative, all were from a low-income area. As stressors such as financial worries (Andrews and Wilding, 2004) and unemployment have been proven to increase anxiety and ill-health (Bartley, 1994), a lack of consideration towards socioeconomic status has the potential to skew results and reduce generalisability.

A small positive association was found between JHS and anxiety in Bulbena and colleagues (2004) cohort study. Participants were employees receiving a medical checkup at a large consultant and legal services company in Barcelona, Spain (n=553). This somewhat unrepresentative sample was invited to take the self-rated Spielberger State-Trait Anxiety Inventory (STAI) and was assessed for hypermobility using the Hospital del Mar criteria. This criteria assesses hypermobility in ten joints using passive movement (the right and left little finger, thumb, elbow, shoulder rotation, hip, knee extension and flexion, patella, ankle and metatarsal-phalangeal joint) in addition to trunk mobility (the ability to place the palms flat on the floor while keeping the knees straight (Ohman *et al.*, 2014). Only one point is given regardless of bilateral or unilateral hypermobility, giving a maximum score of 11 points (Ohman *et al.*, 2014). The Hospital del Mar system has been rated as reliable with good internal consistency and predictive validity, with different scores for each gender (Bulbena *et al.*, 2004). Inter-rater reliability for agreement between the

medical researcher and the rheumatologist was high (0.68-1.0). Patients were blind as to their joint mobility status to minimize bias (Bulbena *et al.*, 2004). However, the limited sample does give rise to some confounding factors; all participants were recruited from the same firm, with similar jobs. Although differences in education level were noted, (93.7% were highly educated) these were not examined. Results showed a small significant correlation between trait anxiety and joint laxity score (r_s=0.16, N=526, p=0.0002). State anxiety showed a minor positive correlation with joint laxity (r_s= 0.11, N=526, p=0.01). While results were modest and difficult to generalise, these findings fit with a previous study of anxiety and hypermobility by (Bulbena *et al.*, 1988, Bulbena *et al.*, 2004).

Likewise, Baeza-Velasco and colleagues (2011) found significant associations between JHS/EDS-HT and anxiety in a cohort study of participants recruited from a French university. Results indicated that women with JHS had a significantly higher anxiety score, as measured by the Hospital Anxiety and Depression Scale (HADS), compared to those without the condition (t = -2.35, p = 0.019). Women with JHS also had higher anxiety scores on the HADS (34.6%), compared to those without JHS (23.6%;(Baeza-Velasco *et al.*, 2011a). Men with JHS did not differ significantly in their HADS scores when compared to controls and showed higher rates of social anxiety, as measured by the avoidance scale of the Leibowitz Social Anxiety Scale (LSAS; t = -2.41, p = 0.01). This indicated that men with JHS may be more avoidant of social situations than those without the condition (Baeza-Velasco *et al.*, 2011a). In addition, men with JHS/EDS-HT also had higher scores for social anxiety on the LSAS (78.6%) compared to controls (41.7%). Women with JHS did not differ significantly in their LSAS scores when compared to controls (Baeza-Velasco *et al.*, 2011a).

Gurer and colleagues (2010) case-control study compared anxiety disorders in patients with GJH (Beighton score ≥4; N=40) to a control group without psychiatric disease or hypermobility (Beighton Score of 0; n=54). A Beighton Score of ≥4 was used to define hypermobility. A psychiatrist, blind to the group status of each participant, screened participants for psychiatric disorders using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and measured anxiety using the Hamilton Anxiety Rating Scale (HAM-A). Results showed that hypermobile participants had higher anxiety levels than the control group. No significant

difference was found regarding panic disorder, major depression, generalised anxiety, and obsessive-compulsive disorder (OCD;(Gurer *et al.*, 2010). Conversely, the study gives very few details regarding how panic disorder, major depression, generalised anxiety and OCD were assessed and evaluated.

In a 15-year follow-up cohort study, Bulbena and colleagues (2011) examined whether JHS is a risk factor for anxiety disorders by assessing participants using the Structured Clinical Interview from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). Participants (n=158) were assessed for hypermobility and anxiety disorders at baseline and at 15-year follow-up. Although a large sample, recruiting from such a narrow population may be difficult, as differences in social and cultural norms may modify outward expressions of anxiety. Results showed that JHS was found in 21.1% of participants at baseline. Incidence of panic disorders was higher for JHS (41.4%) than the control group (2.8%), but rates of generalised anxiety disorder (GAD) were not significant. Rates of panic disorder were also higher for those with JHS compared to those suffering from other chronic musculoskeletal conditions (Bulbena *et al.*, 2011). Turk and colleagues (2010) advised caution when comparing the symptoms of patients with chronic pain to the diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), as in Bulbena and colleagues' (2011) study, as common psychiatric disorders and syndromes could have symptoms that overlap with those of medical conditions.

A recent cross-sectional study by Baeza-Velasco and colleagues (2018) explored the association between high anxiety (as measured by the French version of the HADS), psychosocial factors, health, and sociodemographic factors in participants with hEDS (the equivalent to EDS-HT under the 2017 criteria). Eighty participants' with hEDS were divided into low (scores 2-11 on the HADS) and highly anxious (score ≥11) groups. Results indicated 51.2% of participants scored highly for anxiety, while 20% of participants had depression. Participants in the high anxious group had higher levels on certain scores compared to the low-anxious group, including pain catastrophizing (31.5% vs 17%, P = <0.001) and reduced social functioning (25% vs 50% satisfaction, P = <0.001) compared to the low-anxious group (Baeza-Velasco *et al.*, 2018). However, the cross-sectional design makes it difficult to

draw any inference regarding the direction of relationships, and there is no control group to compare the data, making it difficult to draw reliable conclusions (Baeza-Velasco *et al.*, 2018).

2.13.3 Depression

In addition to anxiety, Smith and colleagues (2014) systematic review and meta analysis also compared studies for the prevalence of depression in those with JHS/EDS-HT, compared to those without the condition. A meta-analysis revealed that overall, those with JHS/EDS-HT were four times more likely to have depression, compared to those without the condition (OR 4.10, 95% CI 1.78, 9.41, P <0.001) (Bulbena and Berrios, 1993, Bulbena *et al.*, 2011, Gurer *et al.*, 2010), but unlike the results for anxiety, when the severity of depression was compared between case and control populations, there was no significant difference (Smith *et al.*, 2014b). Conversely, two studies focusing on dysrhythmia disorders (Bulbena *et al.*, 1993, Gurer *et al.*, 2010) did not find a significant difference between those with JHS/EDS-HT and those without (OR 1.12, 95% CI 0.47, 2.67, *P* = 0.80) (Smith *et al.*, 2014b).

A case-control study by Bulbena and colleagues (1993) found participants with JHS (Beighton score ≥3, or scores of ≥5 items of the Beighton diagnostic criteria) to have significantly higher scores on the Hamilton Rating Scale for Depression (mean= 8.3, SD 6.1, *p*= 0.01), compared to control participants (mean= 6.0, SD 5.1, (Bulbena *et al.*, 1993). However, the 114 cases were not matched with the 59 control participants, and there were significant differences between the groups, in terms of height (159.5 cm, SD 7.7 vs. 153.3cm SD 5.8) and age (48.1 years +/- SD 13.5 vs. 41.8 years +/- SD 13.9, (Bulbena *et al.*, 1993), all of whom were recruited from the same hospital rheumatology department in a low-income area, which may reduce the generalisability of the findings.

A cross-sectional study by Baeza-Velasco et al (2011) explored the frequency of JHS among university students. A sample of 365 undergraduates from a single university were assessed using the Brighton Criteria, Somatosensory Amplification Scale (SSAS), Liebowitz Social Anxiety Scale (LSAS) and the Hospital Anxiety and Depression Scale (HADS; (Baeza-Velasco *et al.*, 2011b). Although the cutoff is typically ≥4/9, the authors acknowledged variation in the Beighton score used in

other studies as between 4 and 6 points out of nine. Therefore, a Beighton cut-off score of ≥5 was used as indicative of GJH (Baeza-Velasco *et al.*, 2011b). Overall, 39.5% of participants met the Brighton criteria for JHS. But, it is not clear how participants were assessed, implying that hypermobility was a self-report measure. Confidence intervals were not reported. Women with JHS showed significantly higher levels of depression on the HADS than women without JHS. Those with greater ratings of physical pain were also more likely to score highly for depression (Baeza-Velasco *et al.*, 2011b), echoing previous links between chronic joint pain and depressive symptoms (Grahame, 2009). Participants with JHS also scored significantly higher on the Somatosensory Amplification Scale (SSAS) than participants without the syndrome (Baeza-Velasco *et al.*, 2011b). An assessment of the SSAS' psychometric properties indicated that the SSAS was a more accurate reflection of participants' general distress, the frequency of 'daily hassles' (*not* relating to health or symptoms) and negative mood, rather than a valid measure of somatic sensitivity (Aronson *et al.*, 2001).

A population-based matched cohort study conducted in Sweden compared 1,771 individuals with EDS-HT to 17, 710 control comparators (Cederlof *et al.*, 2016). Conditional logistic regression indicated associations between EDS-HT and depression: risk ratio (RR) 3.4, 95% CI 2.9-4.1; autism spectrum disorders: RR 7.4, 95% confidence interval (CI) 5.2-10.7; bipolar disorder: RR 2.7, CI 1.5-4.7; ADHD: RR 5.6, CI 4.2-7.4; and attempted suicide: RR 2.1, 95% CI 1.7-2.7, but not for suicide or schizophrenia (Cederlof *et al.*, 2016). Anxiety disorders were not featured as an outcome measure (Cederlof *et al.*, 2016).

In contrast to other positive results, Bulbena and colleagues (2011) and Gurer and colleagues (2010) studies did not find significant differences in the incidence of depression between participants with and without JHS.

2.13.4 Panic disorder

A meta analysis regarding the prevalence of panic disorder in JHS/EDS-HT (Smith *et al.*, 2014b), compared the results from four studies with participants who had JHS (Benjamin *et al.*, 2001, Bulbena *et al.*, 1993, Bulbena *et al.*, 2011, Garcia Campayo *et al.*, 2010). Results indicated that those with JHS/EDS-HT were seven

times more likely to suffer from a panic disorder, compared to those without the condition (OR 6.72, 95% CI 2.22, 20.35, P <0.001, (Smith *et al.*, 2014b).

To assess whether GJH was more frequent in patients with panic disorder than controls, (Garcia Campayo *et al.*, 2010) compared patients diagnosed with a panic disorder (N=55) to three age, ethnicity and sex-matched control groups; healthy controls (N=55), psychiatric controls (N=55), and control patients with fibromyalgia (N=55), as fibromyalgia has been reported to have a high association with GJH. Although the authors have used the term 'JHS' throughout, only the Beighton Score was used during classification, with a cutoff of ≥5/9 indicating GJH. However, without further examination of participants using the Brighton Criteria for a diagnosis of JHS, participants would only be classified as having GJH, not JHS. Psychological variables were assessed using Spanish versions of the State Trait Anxiety Inventory (STAI), Panic and Agoraphobia Scale (PAS) and Hospital Anxiety and Depression Scale (HADS). Assistants and a doctor blind to the scores of each participant assessed joint hypermobility using the Beighton score (≥5/9). The results indicated a significant number of patients with panic disorder met the criteria for GJH (61%), compared to controls with fibromyalgia (25.4%) and healthy controls (11%). Women and younger participants were more likely to have GJH, but this pattern was not replicated with men, or participants aged >45. Although attributed to a small sample size, this result may actually be representative of hypermobility throughout the lifetime: decreasing with age and, due to hormonal differences, having a lesser prevalence in men (Garcia Campayo *et al.*, 2010).

Conversely, when examining patients diagnosed with panic disorder for signs of joint hypermobility, Benjamin and colleagues (2011) failed to find a significant association. The study measured GJH in patients with panic disorder and assessed carbon dioxide reactivity, an indicator of a possible underlying genetic vulnerability towards panic disorder. The sample was a clinically representative population of patients with panic disorder (N=101). By recruiting from three different anxiety clinics in Israel, the authors accounted for any confounding environmental factors. Healthy controls representative of the target population were assessed for joint hypermobility using the Beighton score (using a cutoff of ≥5 to indicate GJH N=39) and carbon dioxide reactivity (N=20). As with Garcia-Campayo and colleagues (2010)

study, although the authors refer to participants as having JHS, without further examination of participants using the Brighton Criteria, participants would only be classified as having GJH, not JHS (Benjamin *et al.*, 2001). Confidence interval data and odds ratios were not presented, preventing an assessment of precision. The authors did not find a significantly higher prevalence of joint hypermobility in patients with panic disorder, and questioned whether this was due to a genetic variation in the Israeli population (Benjamin *et al.*, 2001).

Although a genetic link between panic disorder, social phobia and joint hypermobility was proposed, this association proved unpredictable (Gratacos *et al.*, 2001), and the validity of Gratacos and colleagues (2001) data and findings have been questioned by successive studies, none of which were unable to detect any positive trace of DUP25 in patients with anxiety disorders (Henrichsen *et al.*, 2004), panic disorder (Zhu *et al.*, 2004) or in genetic samples from control participants (Tabiner *et al.*, 2003, Zhu *et al.*, 2004).

2.13.5 Fears and phobias

Despite studies showing JHS to be associated with more intense fears, the clinical significance of such positive findings remains uncertain. Bulbena and colleagues (2006) examined participants using a Beighton score cutoff of ≥4/9. However, as participants were not assessed for JHS using any form of formal diagnostic criteria, it is difficult to ascertain whether participants had GJH or JHS. Ratings of fear and fear intensity were found to be comparable between participants with JHS and control participants (Bulbena *et al.*, 2006). Fear intensity and frequency was assessed using a modified version of the Fear Survey Schedule (FSS-III), with more intense fears compared between hypermobile and non-hypermobile participants. GJH was found in 19.9% of women and 6.9% of men. Mean total scores were significantly higher for both genders in the hypermobile group. Fears also varied by age, with women over 50 reporting more intense fears of falling and crossing the street than those under 50 (Bulbena *et al.*, 2006).

Bulbena and colleagues (2011) found a significant incidence of social phobia in JHS participants (24.1% JHS, 3.7% control) and simple phobia (27.6% JHS, 8.3% control). JHS was assessed using the Beighton Score and the Brighton Criteria for JHS

(Grahame *et al.*, 2000). Although there was no significant difference in the predisposition between men and women to suffer panic disorders, analysis of the predisposition to feel fear did show gender-related differences, with women having a greater number of more intense fears than men (Bulbena *et al.*, 2011). Initially no significant differences were obtained in LSAS scores between participants with and without JHS, however when adjusted for gender a weak positive result was obtained for men with JHS avoiding social situations. However, the limited sample size (N=68 male JHS participants) limits the generalisability of this result.

Studies examining a link between fear and JHS/EDS-HT both used the Fear Survey Schedule to assess common fears and phobias (Bulbena *et al.*, 2006, Pailhez *et al.*, 2011). While Smith and colleagues (2014) found that there was insufficient data to pool the results, the findings did indicate higher fear scores (91.6, $P = 0.005$), compared to those without JHS/EDS-HT (11, N.S;(Pailhez *et al.*, 2011). A similar findings was found for (Bulbena *et al.*, 2006) for those with JHS/EDS-HT, compared to controls (83.7 *vs* 66.3, $P = 0.005$).

Although these results do show some significant differences relating to the intensity of fears between GJH JHS and control participants -and men and women in relation to fears- the fears presented appear to be common worries shared by many people, often with links to human survival, such as fears of death, open wounds, cadavers, serious injury, being alone, ignored, and rejected socially by others (a potentially disastrous fate for humans in early communities, who would have relied on social groups for survival; (Eisenberger and Lieberman, 2004). It may be more clinically significant to investigate patients' fears relating to activity and movement (kinesiophobia), as this can be associated with decreased muscle tone and a decline in overall levels of functioning (Grahame, 2009, Ross and Grahame, 2011). Indeed, fear of potential physical injury and having increased pain was cited as a reason for patients with EDS-HT deliberately avoiding potential high-risk activities such as sports and regular exercise (Rombaut *et al.*, 2010).

2.13.6 Social functioning

In addition to the substantial emotional impact outlined above, adults with JHS/EDS-HT have also been found to have decreased physical and social functioning as a result of their symptoms. A survey of 32 women with EDS-HT were found to have significantly lower participation in physical activity and sport when compared to control participants, but around the same amount of leisure time as control participants (Rombaut *et al.*, 2010). This reduced participation was estimated to be due to fear of injury, having increased pain (Lumley *et al.*, 1994), or possibly reduced physical fitness. However, the reasoning for participants' reduced participation in physical activity was not explored (Rombaut *et al.*, 2010).

Participants were also found to have significantly lower scores on the RAND-36 Health Survey when compared to a control group ($p<0.001$), indicating poor health-related quality of life (HRQoL), and substantial impact on their physical, emotional and social functioning (Rombaut *et al.*, 2010). In addition, the study only examined the experiences of women with EDS-HT. Although JHS/EDS-HT typically affects more women than men, it is not clear whether men with the condition would have given different results, or have experienced different social pressures to engage in sport or physical activity as a result of their gender and societal expectations. For example, in Western societies, men are encouraged to construct their identity in relation to sport and physical activity (Lee *et al.*, 2009), with those who display high sporting ability in sports such as football often awarded a higher status of masculinity (Phoenix and Frosh, 2001).

The psychosocial impact of JHS/EDS-HT has also been recognised in education and the workplace. Some adults with EDS described their school years as difficult, due to teasing from other children (Lumley *et al.*, 1994) or a lack of understanding of the symptoms of EDS from various teachers, particularly during physical education (Berglund *et al.*, 2000). Those with JHS/EDS-HT have described work as physically or emotionally draining, but often took care to hide their symptoms and the impact of the condition from others in the workplace, in order to avoid perceived discrimination and negative consequences (Berglund *et al.*, 2000, De Baets *et al.*, 2017).

Fear of injury has also been reported by those with EDS as making them less socially active than they would like (Lumley *et al.*, 1994). Indeed, highly anxious patients with hEDS had significantly poorer social functioning, and higher levels of pain catastrophising and somatosensory amplification (a hyper-vigilance to mild somatic and visceral sensations, and a tendency to interpret these sensations as pathological) compared to those with hEDS and lower levels of anxiety (Baeza-Velasco *et al.*, 2018). However, due to the lack of qualitative feedback from participants in this study it is not clear whether the poor social functioning was due to restrictions due to symptoms of pain from hEDS (making it more difficult to meet and socialize), restrictions due to high anxiety (making participants more reluctant to socialise) or a combination of both. Further qualitative research is needed to explore the psychosocial impact of JHS/EDS-HT, including emotional and social support from friends and family, and how participants with JHS/EDS-HT could utilise these to cope with their condition.

In many studies examined thus far, the emphasis has been on psychological differences; little attention is paid to understanding the patient's own experience of the syndrome and how best to improve quality of life. This study aims to expand the existing psychological literature relating to hypermobility syndromes by providing a greater understanding of how JHS/EDS-HT affects the patients who experience these syndromes, and how best they can cope with these problems to better self-manage their condition.

2.14 Treatment strategies for JHS/EDS-HT

To this point, this thesis has primarily explored the physical, and psychosocial impact of JHS/EDS-HT on men and women. While there is currently little research evidence regarding treatment strategies for those with JHS/EDS-HT, it is recognised within the literature that physiotherapy and therapeutic exercise are important elements of treatment and rehabilitation (Palmer *et al.*, 2014), and if implemented effectively, rather than 'spiralling' into poorer functioning (Grahame, 2009), effective treatment can result in improvements both to patients' functional ability and their quality of life (Simmonds and Keer, 2007).

In order for the best possible treatment outcomes, it is important that GPs and allied health professionals have a good knowledge and awareness of JHS/EDS-HT (Russek *et al.*, 2019). Research has indicated a lack of awareness of hypermobility within primary care (Lumley *et al.*, 1994), (Schmidt *et al.*, 2015), and GPs historically have reported a lack of confidence in performing musculoskeletal examinations (Abou-Raya and Abou-Raya, 2010, Coady *et al.*, 2004, Day and Yeh, 2008, Goff *et al.*, 2016). People with JHS/EDS-HT have highlighted persistently long waits for diagnosis of their condition, often of several years since first experiencing symptoms (Bovet *et al.*, 2016, Palmer *et al.*, 2016b, Terry *et al.*, 2015), which may worsen physical and psychosocial functioning as chronic pain, and associated psychological distress, becomes more of a problem (Palmer *et al.*, 2016b, Smith *et al.*, 2014b). The general lack of training and awareness regarding JHS/EDS-HT within medical practice has been described as the biggest barrier to the successful management of JHS/EDS-HT (Berglund *et al.*, 2010, Grahame, 2008).

It has been argued that healthcare professionals need to be able to effectively recognise the wide range of systemic issues that can affect people with JHS/EDS-HT, in order to promote understanding of the condition, and the best possible treatment outcomes (Russek *et al.*, 2019). Factors that may have a significant impact on people's lives, though not included within the diagnostic criteria for JHS/EDS-HT at present, should also be considered during treatment and rehabilitation, such as Postural Orthostatic Tachycardia Syndrome (POTS), sleep disturbances, fatigue, issues with digestion, anxiety or depression (Malfait *et al.*, 2017).

Although physiotherapy is considered a fundamental treatment option for JHS/EDS-HT, and that regular exercise is beneficial, there has been a lack of evidence regarding the type, frequency or means of delivery of physiotherapy-based interventions recommended for those with JHS/EDS-HT (Simmonds and Keer, 2007, Smith *et al.*, 2014b).

In order to better support the treatment of patients with JHS/EDS-HT, the management of JHS/EDS-HT in adults, adolescents and children needs to be based on the best evidence available (Engelbert *et al.*, 2017, Russek *et al.*, 2019).

Principles of management cover a range of options, but improvements to muscle strength and proprioception can be beneficial in reducing JHS/EDS-HT related pain (Russek *et al.*, 2019). These have included gradually progressive exercises guided by motor learning theory to ensure effective movements (Palmer *et al.*, 2016b, Smith *et al.*, 2014b). Based on experience with patients with JHS/EDS-HT, Russek, Stott and Simmonds (2019) recommend rehabilitation activities such as patient education regarding body mechanics and injury prevention (Russek *et al.*, 2019). One randomised control trial involving exercises to improve proprioception, balance and muscle strength demonstrated reduced knee pain and increased proprioception in those with JHS/EDS-HT, compared to a control group (Sahin *et al.*, 2008).

Small pilot studies of intervention options, such as inpatient rehabilitation programmes and strengthening exercise interventions have provided encouraging results (Engelbert *et al.*, 2017). One multidisciplinary programme combined physical and cognitive behavioural therapy for 12 women with JHS/EDS-HT and comprised a 2.5-week stay in an inpatient rehabilitation unit, before being sent home with exercises with weekly guidance from a physiotherapist. Participants showed significant improvement in performance of daily activities, improved muscle strength and endurance and decreased kinesiophobia (Bathen *et al.*, 2013).

A home-based exercise programme comprised an 8-week programme of progressive closed kinetic chain exercises, and assessment of physical functioning and psychological health using the SF-36 questionnaire (Ferrell *et al.*, 2004). After the intervention, 16 of 18 participants showed improvements in knee joint proprioception (as measured by a threshold detection paradigm), muscle strength and balance. Following the programme, participants also showed significant improvement in physical functioning (P =0.029), mental health (P = 0.008) and role limitation due to emotional problems (P = 0.019, (Ferrell *et al.*, 2004). However, there were no significant improvements in social functioning or energy and vitality as measured by the SF-36, indicating that further interventions targeting these factors may be beneficial in order to support participants with JHS/EDS-HT. In addition, without a control group, it is difficult to compare these results to a population without JHS/EDS-HT.

An outpatient pain management programme also showed promising results for patients with JHS/EDS-HT (Rahman *et al.*, 2014). The programme of 8 days was spread over 6 weeks, delivered by two rheumatologists, two clinical psychologists, one nurse and one physiotherapist. Patients were invited to set individual goals to work towards. At baseline, 1 and 5-month follow up, assessments were made of pain intensity, self-efficacy, catastrophizing, frustration, depression and anxiety. At five-month follow-up, participants showed significant improvements in pain catastrophizing (P = <0.001), impact on daily life (P = <0.001), frustration (P = <0.001) and smaller improvements in scores for anxiety (P = 0.013), depression (P = 0.015) and self-efficacy (P = 0.002,(Rahman *et al.*, 2014). However, there are a number of limitations to this study, firstly that only 50% of the original cohort were available to be re-tested at five-month follow up, and the reasons for such a large attrition rate were not explored. Secondly as with Ferrell and colleagues (2004) study, there was no control group or non-intervention JHS group to compare the results to, which would have given a better overview of any effects in a larger group context. As such, Engelbert and colleagues argue that these interventions need to be further evidenced by more rigorous research designs (Engelbert *et al.*, 2017).

Due to the potential complexity of patients with JHS/EDS-HT, a number of recent articles have recommended the implementation of comprehensive, multidisciplinary models of care for hypermobility (Bulbena *et al.*, 2017, Palmer *et al.*, 2014). However, access to JHS/EDS-HT-specific management services is very geographically limited in the UK and there are few options for multidisciplinary care. The London Hypermobility Unit is a specialist UK centre for the diagnosis, assessment, and management of hypermobility-related disorders. It is unique in its provision of specialist multidisciplinary service and comprehensive assessment of patients presenting with hypermobility (Keer *et al.*, 2015). A clinical audit and patient satisfaction survey indicated that 100% of patients had a diagnosis of JHS/EDS-HT, with 41% referred onto other therapies. As with the models of care outlined above, patient satisfaction was very high, with 85% of patients very satisfied with the service, and 96% reporting that they felt that the physiotherapist understood the problem. However, patients reported significant dissatisfaction with long waiting times for the private service (Keer *et al.*, 2015). Only The London Hypermobility Unit,

The Royal National Orthopaedic Hospital, Stanmore and the University College London (UCL) Department of Rheumatology have dedicated practice for the diagnosis and management of patients with JHS/EDS-HT. This exclusivity may not only increase waiting times for diagnosis, but also substantially limit the opportunities for patients with severe JHS/EDS-HT in more geographically remote locations to access specialist services.

Efforts have been made to improve recognition of JHS/EDS-HT in primary care, with the publication of the Ehlers-Danlos GP toolkit, a collaboration between GP and JHS/EDS-HT researcher Emma Reinhold and the EDS patient support group Ehlers-Danlos Support UK (EDS-UK) (Reinhold *et al.*, 2018). The toolkit provides a guide to GPs to the symptoms and management of EDS, signposting to resources for patient support, as well as giving indications for onward referral (Reinhold *et al.*, 2018).

However, with potential for such marked differences in the diagnostic accuracy, referral, treatment pathway, delivery and type of care offered to patients, this can result in unreliable and fragmented care for people presenting with JHS/EDS-HT. This patchy treatment may lead to poor outcomes for patients, significant psychological distress, and by association substantial healthcare costs to the NHS.

2.15 Rationale for the current study

It is clear from the research outlined above that adults with JHS/EDS-HT experience a wide range of symptoms, including joint pain, joint dislocations and fatigue. Research has also indicated a substantial emotional component, including significant anxiety, depression, panic disorder, fears and a low quality of life.

Through evaluation of the literature above relating to emotional support needs, and the lack of supportive treatment from the NHS to manage JHS/EDS-HT, it is clear that there is a lack of psychosocial support for patients. Despite publication of the Ehlers-Danlos GP toolkit (Reinhold *et al.*, 2018), recognition of JHS/EDS-HT, and associated conditions within primary and secondary care remains poor (Russek *et al.*, 2016). In addition, it seems that men and women with JHS/EDS-HT are not

informed regarding the potential impact of the condition on their lives following diagnosis, or the potential impact and complications regarding other significant life events such as pregnancy (Pezaro *et al.*, 2018).

A final psychosocial consideration is the impact of living with an unseen condition. Like other chronic pain conditions, because the symptoms of JHS/EDS-HT (such as joint pain or fatigue) are not immediately visible to others, it can be described as an 'invisible illness'. This indiscernibility can leave people with invisible conditions more likely to experience negative reactions from others, such as disbelief, unwanted intrusion from strangers and a lack of social support from friends and family (Brennan and Creaven, 2016, Moses *et al.*, 2005, Juuso *et al.*, 2014, Mazzoni and Cicognani, 2014). In Brennan and Creaven's (2016) study, participants with lupus reported a lack of understanding of their condition from others, which caused them to feel lonely and despondent. Similarly, women with Fibromyalgia, another invisible condition, were not seen as credible and often faced questioning regarding the legitimacy of their illness in their family, social and work lives (Juuso *et al.*, 2014). Indeed, the idea that others around them do not believe their symptoms can be "*a heavier burden than the illness itself*." (Asbring and Narvanen, 2002) p.152). When others acknowledged their invisible condition and treated them with respect, women reported feeling valued and stronger (Juuso *et al.*, 2014). While this literature makes it clear that for some, an invisible illness such as Fibromyalgia, lupus or osteoarthritis can be a disadvantage, care was taken not to assume a totally negative position, as unlike patients with obvious visible differences such as scarring or amputation, those with invisible illness have the ability to hide their condition from others. This can be used to their advantage when not wishing to disclose their condition, or, when they wish to appear as 'normal' (Goffman, 1963, Joachim and Acorn, 2000). However, passing for normal can create additional stress, due to the risk of discovery and fears concerning the potential embarrassment of being caught (Goffman, 1963). Therefore, in the present study, it will be vital to examine participants' views and experiences relating to invisible illness, as have been achieved in other chronic pain conditions.

A number of researchers have expressed a desire for greater psychosocial support for this population, including the need for more individualised care and

support (Baeza-Velasco *et al.*, 2015, Berglund *et al.*, 2015, Hakim *et al.*, 2017, Scheper *et al.*, 2017). For example, Berglund and colleagues (2015) indicated an unmet need to learn about the daily consequences of EDS, particularly to "*acknowledge the physical and psychosocial differences*" (Berglund *et al.*, 2015) p. 4) for this population, all of whom will experience JHS/EDS-HT as a lifelong, genetic disease (Berglund *et al.*, 2015). Perhaps the most compelling recommendation for research comes form (Baeza-Velasco *et al.*, 2018), who argued in their implications for rehabilitation that exploring the psychosocial functioning of patients was vital as part of an overall chronic pain and treatment management strategy in EDS-HT, as has already been achieved in other chronic pain conditions.

Despite the long-term awareness and prominent recognition of psychosocial dysfunction in EDS (Cederlof *et al.*, 2016), there is a lack of research into the psychosocial, cognitive and behavioural impact of JHS/EDS-HT on adults' lives. Research into the psychosocial impact of the condition is important to better support those with the condition in their day-to-day functioning, and any additional support needs they may have. As argued by Kalisch and colleagues (2019), it is the marked differences and variability in psychosocial and health-related variables that predict pain and physical disability in adults with JHS/EDS-HT (Kalisch *et al.*, 2019). Through better identifying and understanding the psychosocial impact, researchers have an improved chance to provide focused, targeted prevention and intervention programmes to patients with JHS/EDS-HT (Kalisch *et al.*, 2019).

2.16 Summary

This chapter has outlined the history and diagnostic criteria for JHS/EDS HT and critically evaluated the updated 2017 hEDS diagnostic criteria (Malfait *et al.*, 2017). The prevalence of GJH using the five-part questionnaire for hypermobility (5PQ; Hakim and Grahame, 2003) and the Beighton Score were explored, including variations in GJH observed within populations depending on age, gender and ethnicity. The psychological impact of JHS/EDS-HT was explored, in terms of anxiety, depression, fear, and panic disorder, with a broad range of studies indicating substantial psychological distress. Lastly, treatment options and potential barriers to

effective management of JHS/EDS-HT were considered, highlighting a gap in the research and the need for holistic, targeted, multidisciplinary care for this population.

Results indicate that participants with JHS/EDS-HT are four times more likely to suffer from an anxiety disorder compared to control participants without hypermobility (Smith *et al.*, 2014b). Despite claims of a genetic link between JHS/EDS-HT and panic disorders (Gratacos *et al.*, 2001), the integrity of this research has been called into question by several authors, (Henrichsen *et al.*, 2004, Zhu *et al.*, 2004). Instead, a link between symptomatic hypermobility, POTS and dysautonomia and anxiety-related symptoms may be able to account for a high prevalence of anxiety disorders in those with JHS/EDS-HT compared to other musculoskeletal conditions (Wells *et al.*, 1988). Regardless of the potential genetic prevalence, qualitative research is needed to explore potential reasons and mechanisms in patients' lives that may be exacerbating their anxiety, depression and contributing to feelings of panic and fear. Exploring the root of participants' fears and anxieties (Bulbena *et al.*, 2011) and whether targeted, supportive behaviour change interventions could help patients with JHS/EDS-HT to better manage the psychosocial impact.

While studies examining the psychological impact of JHS/EDS-HT have been published, there are a number of limitations to the literature. Populations chosen from rural, geographically isolated areas (Bulbena *et al.*, 2006), low-income populations (Martin-Santos *et al.*, 1998), a single university (Baeza-Velasco *et al.*, 2011a), or workplace (Bulbena *et al.*, 2004) may reduce generalisability and prevent richer analysis of data (Bulbena *et al.*, 2011). Therefore, conducting research with a purposive sample of participants from a variety of socioeconomic, educational and geographical backgrounds could have the benefit of improve the generalisability of this research to a UK population.

In conclusion, these studies emphasise the importance of an integrated approach to the management of EDS/JHS patients. Effective understanding and the early detection of hypermobility and provision of support, treatment and information may help participants to self-manage their condition over time.

2.17 Thesis aims:

To recap, the overarching aims of this thesis are:

- To understand the lived experiences of people with JHS and EDS.
- To explore the psychosocial**,** cognitive and behavioural impact of JHS/EDS-HT.
- To determine the components of a behaviour change intervention for people with JHS/EDS-HT.

The thesis has been designed in three phases to address these aims. The decision and reasoning for using a mixed methods design has been explored in Chapter 3, Methodological Considerations. The three phases are:

1. Study 1 (Chapter 4): Firstly, a qualitative systematic review of the literature explores patients' lived experiences of JHS and EDS in daily life by pooling the results of published studies and re-analysing in a thematic synthesis to draw out similar themes across the published studies.

2. Study 2 (Chapter 5): Secondly, qualitative semi-structured interviews with adults who have JHS/EDS-HT explore the psychosocial, cognitive and behavioural impact of the condition, and identify different methods of coping and how participants manage their condition.

3. Study 3 (Chapter 6): The results from Study 1 and Study 2 are mapped to behaviour change theory, The Theoretical Domains Framework and capability, opportunity, behaviour model (COM-B, (Michie *et al.*, 2011). The results of this mapping, a series of potential behaviour change interventions, are presented to a new cohort of participants in two focus groups. Finally, participants are asked to identify and quantitatively rank which behaviour change interventions are most important to them, using a modified Nominal Group Technique (NGT). From these combined qualitative and quantitative findings, potential interventions to support participants with JHS/EDS-HT are identified.

3 Chapter 3: Methodological considerations

3.1 Background

This chapter provides an overview of the methods used to conduct the research. Firstly, decisions and reasons underpinning the use of mixed methods are discussed, including the evolution of mixed methods over time into a 'third paradigm' of pragmatism. The choice of a multiphase sequential design is justified. Next, reflections on my own 'dual role' as both an insider and outsider to JHS/EDS-HT research are considered. Lastly, issues relating to participant sampling and the benefits and associated challenges in researching a hard-to-reach population are considered, along with the strategies put in place to aid recruitment.

3.2 Using mixed methods in research

Described as the third research paradigm (Johnson *et al.*, 2007, Dures *et al.*, 2011), mixed methods research has been cited as offering a fuller alternative to purely qualitative or quantitative research alone. Combining and amalgamating qualitative and quantitative data can raise a number of challenges, however, including difficulties around definitions of the term and a lack of approved guidance as to how to conduct mixed methods research, or how to successfully integrate qualitative and quantitative data together (Creswell *et al.*, 2004, Anguera *et al.*, 2018). Creswell (2015) defined mixed methods studies as:

> "An approach to research in the social, behavioural, and health sciences in which the investigator gathers both quantitative (closed-ended) and qualitative (open-ended) data, integrates the two, and then draws interpretations based on the combined strengths of both sets of data to understand research problems."
>
> (Creswell, 2015, p.124)

In this case, Creswell indicates that to mix methods involves integration of both quantitative and qualitative data, with interpretations drawn based on both in order

to better answer the research question (Creswell, 2015). As argued by Anguera and colleagues (2018), research should ideally move beyond a solely descriptive analysis in order to contribute to a greater understanding and interpretation of observed phenomena (Anguera *et al.*, 2018).

3.3 Paradigm struggles and mixed methods

Qualitative and quantitative approaches have long been associated with distinct paradigmatic approaches to research. Researchers have historically been divided between positivist (quantitative) researchers and constructivist or interpretivist (qualitative) research. Qualitative and quantitative research has typically been presented as embodying very different assumptions in relation to epistemologies (ways of knowing and understanding) and ontologies (assumptions about reality and the nature of reality (Dures *et al.*, 2011). Epistemology can been defined as the theory of knowledge and exploring the extent to which scientific theories are true (Ladyman, 2013, Dures *et al.*, 2011). Ontology is the study of being, and the view of reality (Dures *et al.*, 2011). All kinds of things exist, but ontology focuses on the objects within science. These realities can be divided into things that are observable, and things that are not, such as abstract concepts (Ladyman, 2013). From the 1970s to the 1990s, advocates of qualitative and quantitative research had been engaged in ardent debate regarding the relative mismatch of the methods and approaches, termed the "paradigm wars" (Johnson and Onwuegbuzie, 2004, Bazeley, 2004). The war was fuelled by the belief that the positivist/post positivist and constructivist/interpretivist paradigms were inherently incompatible and could never be used together due to their inherent philosophical differences (Tashakkori and Teddlie, 2003).

Quantitative purists, under what is termed a postivist philosophy, believe that social observations should be treated as separate entities, in the same way that scientists treat various phenomena, and that the researcher, as an observer, is completely separate from the entities that they are choosing to observe (Johnson and Onwuegbuzie, 2004). With this stance, researchers typically remain emotionally removed from their participants in order to fully investigate or defend their

hypothesis. Writing is characteristically objective, in the passive voice and using technical terminology (Tashakkori and Teddlie, 1998, Johnson and Onwuegbuzie, 2004). Research methods are typically survey-based or through use of closed-ended questionnaires, with the aim being to test a hypothesis and measure patterns or relationships between different variables (Maxwell *et al.*, 2017). Although a useful standpoint from a scientific perspective, much of the research within JHS/EDS-HT had been conducted using a quantitative, positivist philosophy. While these have undoubtedly provided valuable results regarding people with JHS/EDS-HT and psychological issues such as anxiety (Bulbena *et al.*, 1993, Martin-Santos *et al.*, 1998), depression, and fear (Bulbena *et al.*, 2006, Castori *et al.*, 2010, Hakim and Grahame, 2003, Hakim *et al.*, 2004, Bulbena *et al.*, 2011, Rombaut *et al.*, 2011a, Scheper *et al.*, 2016, Smith *et al.*, 2014b) these results did little to rationalise, or give explanations for, differences in the experiences of people with JHS/EDS-HT or reasons *why* participants with the condition may be more anxious, depressed or fearful when compared to the general population. Indeed, Crossley (2000) argues that quantitative questionnaires cannot effectively reflect the multiple realities of people's illness experiences (Crossley, 2000).

Conversely, the qualitative paradigm is based on and constructivism and interpretivism (Denzin and Lincoln, 2011). Constructivism involves seeking to undertake research in natural settings (Appleton and King, 2002, Guba and Lincoln, 1982, 1989), with the goal of understanding the complexities of 'lived experience' from the perspective of those who live it (Denzin and Lincoln, 2011). Interpretivism argues that truth and knowledge are culturally and historically subjective, based on people's experiences and understanding (Ryan, 2018). Interpretivism has a 'relativist' ontology, suggesting that reality is only knowable through socially constructed meaning, and there is no shared reality (Ritchie and Lewis, 2003). For example, each person with JHS/EDS-HT receiving treatment in a hospital environment is likely to experience their own unique perception and experience of their treatment, based on their own previous experiences in similar settings, interactions with staff, family members and visitors.

For the present study, a mixed qualitative and quantitative approach offered a number of advantages over a purely quantitative or qualitative method in

isolation. These included the opportunity as a researcher to examine in detail the variety of people's experiences as they participate and interact within their own social worlds (Appleton and King, 2002). By using qualitative methods, phenomena that had been touched upon using quantitative methods in prior studies could be described in richer detail, exploring how these phenomena play out in participants' own naturalistic settings and in their interactions with others (Johnson and Onwuegbuzie, 2004). This was an especially important consideration in order to explore psychosocial, cognitive and behavioural interactions with others in the present study.

In addition, it was imperative for the researcher that participants were involved, not just in a tokenistic or participatory capacity but as true partners in the research, to establish dialogue, and value the experiences of those from groups that have not had a voice in the past (Tashakkori and Teddlie, 1998). The need to use a broad range of qualitative findings was also recognised, in order to recommend potential changes to provision and support for this group of patients, as these qualitative results would be the driving force behind any recommendations for future change. The need for a study design that was qualitatively driven was recognised, but with options for quantitative input as well. By employing mixed methods, not only could a detailed understanding of an under-researched topic be achieved, but triangulation of the qualitative findings across the chapters was also achievable, in order to gain the most comprehensive understanding possible.

With this intention in mind, some limitations of the qualitatively driven design were noted. Primarily, within research there can still be a degree of bias against qualitative research, which can be seen as 'unscientific', 'journalistic', or a 'soft science' compared to quantitative methods (Denzin and Lincoln, 2011). Although previously dominated by quantitative methods such as randomised controlled trials, there has been a growth in popularity of qualitative research within healthcare and the NHS (Maltby *et al.*, 2015). In light of this bias, and the historical prejudice against qualitative research, there was an awareness of the need to be able to instil rigour into the qualitative research.

3.4 Reflexivity in qualitative research

Although involving participants as partners in the research process could be considered a methodological strength, there were some limitations to be considered, including how the researcher's own views and experiences influence the data collection and analysis. How these were considered and addressed to ensure methodological rigour are outlined below.

Reflexivity, an important consideration in qualitative research, is based upon the notion that a researcher's background, perspective and position will affect the topic they choose to investigate, the methods judged most accurate for the purpose, the findings considered most appropriate and the framing and communication of conclusions (Malterud, 2001). Reflexivity is important when using a pragmatic approach, and the need to explore how the researchers own values influence the research (Yvonne Feilzer, 2010). Mays and Pope (1999) maintain that reflexivity requires researchers to be aware of the role that personal characteristics, previous experiences and biases could play in influencing data collection and analysis, including the "distance" between the researcher and those researched (Pope and Mays, 1999). Steier (1991) argues that reflexivity requires us to be conscious of ourselves, a 'bending back' of one's experience on oneself highlighting how we are part of the systems we study (Steier, 1991).

Although I have a Master's degree in Health Psychology, I also have a considerable medical history, having been born prematurely at 25 weeks. I was diagnosed with Ehlers-Danlos Syndrome Hypermobility Type and Postural Orthostatic Tachycardia Syndrome (POTS, a common co-diagnosis in JHS/EDS-HT) in my mid-20s. While some of the problems I experienced, such as recurrent fainting, joint injuries and instability, dental crowding, a large abdominal hernia (nicknamed 'lumpy'), and my long-limbed '*Marfanoid*' body type are fairly typical of JHS/EDS-HT, I have also experienced health events at the more life-threatening end of the spectrum, including a stroke, heart defect and arrhythmias, lung collapse, oesophageal scarring, bowel rupture and associated complications.

As the present thesis and my interactions with participants were about their own lived experiences, not my own, I was wary of including too many details about

myself. However, as an 'insider' to the world of Ehlers-Danlos, I wanted to alter the power imbalance so often seen in traditional research, where the researcher occupies an unspoken position of greater power in comparison to the research participant (Okely *et al.*, 1992, Braun and Clarke, 2013b). I chose to reveal that I have EDS-HT at the start of each interview in Study 2 and each focus group in Study 3, but emphasised that my experiences were likely to be very different from my participants, and it was their own stories that mattered. Although initially cautious that that this would be unprofessional of me as a researcher, I subsequently read several examples where researchers' own insider status within the research topic had been positively addressed (Clarke *et al.*, 2004, Kitzinger and Willmott, 2002). Although I could have kept this from participants, acknowledging my dual identity both as a researcher and a patient, this appeared to instil greater confidence in participants and they seemed very willing to share their experiences:

> "It's nice to speak with somebody who has some knowledge of how it actually feels, because it's like, 'Oh right? What's that?' you know? And they don't really understand."
>
> [Anna, Interview 014]

> "It's nice to have someone who ... genuinely understands it."
>
> [Wendy, Interview 015]

Power can take many forms, whether differences in gender, income, education, health, ethnicity, class or age. However, a similarity in one sphere does not necessarily make a researcher an insider (Tinker and Armstrong, 2008). As Mercer (2007) argues, I found my insider-outsider position to be sited along a spectrum (Mercer, 2007), whereas in one sense I was an insider with a similar diagnosis to my participants, in other contexts I was very much an outsider, such as discussing experiences of motherhood or pregnancy, or men's experiences of JHS/EDS-HT and impact on their masculinity. Dwyer and Buckle's (2009) take on the

insider-outsider locus suggests that the core ingredient of successful research is not how close the researcher is to being an insider or outsider, but their:

> "Ability to be open, authentic, honest, deeply interested in the experience of one's research participants, and committed to accurately and adequately representing their experience."
>
> (Dwyer & Buckle, 2009, p.59)

Consequently, being an insider or outsider does not make for a 'better' or 'worse' researcher, but a different kind of researcher (Dwyer and Buckle, 2009). In light of my need for reflexivity in the research process, I kept a reflective practice log during all data collection and analysis phases.

3.4.1 Reflexivity and rigour

A number of additional processes were put in place to ensure rigour during the data collection phases of the research. At the qualitative interview stage (Study 2), although my position as both a patient and a researcher could be considered a strength, the researcher was also aware of the possibility of bias as a result of this dual position. While bias cannot be eliminated entirely, it can be mitigated (Malterud, 2001). In order to counteract this, I kept a reflective practice research diary exploring my feelings and reflections after each interview. A random selection of recordings was checked against transcripts by the research team (NW, TM, SP), thereby allowing those not directly involved in data collection to audit the results, reducing potential bias, and ensuring accuracy (Malterud, 2001). Peer debriefing was used to safeguard externality, where the research team (NW, TM, SP) reviewed the findings and themes identified in the results. This allowed me the chance to think more critically about the research, and to discuss and explore judgments made about the data. My Director of Studies and I (SP and SB) independently assessed the quality of the Study 2 qualitative interview results using the consolidated criteria for reporting qualitative research (COREQ) framework; a 32-item checklist for reporting interviews and focus groups (Tong *et al.*, 2007). The COREQ questionnaire covers a range of domains relating to openness and disclosure of information about the

research team, including personal characteristics such as their gender, occupation and experience or training, the relationship established between the interviewer and participants, the data analyses and findings (Tong *et al.*, 2007). Overall, incorporating these processes into data collection and evaluation ensured excellent rigour and awareness of reflexivity.

3.4.2 Sampling considerations in hard-to-reach populations: The importance of Patient Research Partner (PRP) and support group partnership

Within the context of health research, hard-to-reach populations can be defined as those who are difficult to involve in research or public health programmes, either due to their social and economic situation, their geographical location or physical disability (Shaghaghi *et al.*, 2011, Sydor, 2013, Krops *et al.*, 2019). Even if accommodations are made for participants, many with severe disability may find attending face-to-face research sessions more difficult, making these potential participants harder to reach (Smeltzer, 2007).

Networking within hard-to-reach communities and the use of social media marketing, community outreach and snowball sampling have been found to be very successful methods of gaining access and participation from invisible communities (Mclean *et al.*, 2003, Uybico *et al.*, 2007, Aldana and Quintero, 2008). In order to ensure that as wide a range of participants with JHS/EDS-HT were engaged and aware of the study as possible, this research programme enlisted the help of two national UK support groups for JHS/EDS-HT: The Hypermobility Syndromes Association (HMSA) and Ehlers-Danlos Support UK (EDS-UK). Both are UK-based support group charities with a wide social media presence, regional in-person support groups and both have been involved in research promotion and recruitment for JHS/EDS-HT in the past.

Both support groups advertised Study 2 and 3 on their social media pages, and these results are detailed in Chapters 5 and 6. The opportunity to take part in a research study for JHS/EDS-HT received very positive feedback and enthusiasm on social media, and 311 participants from the UK and internationally expressed an interest in taking part in the qualitative interview study. The study design and timing had only accounted for a potential participant cohort of between 15 and 20 people,

using semi-structured telephone interviews. For this reason, a purposive sampling strategy was implemented, where participants were selected due to particular representative characteristics, which can be particularly valuable in under-researched populations (Patton, 1990). Participants were actively sought out to provide the best exploration of the research question from a broader variety of cases, as opposed to those that may be the most representative or 'typical' of a JHS/EDS-HT population (Denscombe, 2010, Miles and Huberman, 1994). For example, many of the participants who expressed interest were women in their 30s or 40s with JHS or EDS-HT, and of white ethnicity. These women's experiences are likely to differ from those of older women, women from black and minority ethnic (BME) populations and men with JHS/EDS-HT, whose experiences are very under-represented in JHS/EDS-HT research to date.

This unanticipated positive social media response may have been due to the remote telephone-based nature of the research project, which gave participants the option to take part in the study remotely regardless of their level of disability. Despite recruiting using the same methods for the face-to-face Nominal Group Technique focus groups in Study 3, participants had greater difficulties attending the groups, possibly due to the need to travel to each event. This is an important consideration for future research with JHS/EDS-HT populations, to ensure fair and representative attendance by all.

3.4.3 Qualitative research with remote participants

The second study of this research (Chapter 6) used a qualitative telephone interview methodology to explore the psychosocial, cognitive and behavioural impact of JHS/EDS-HT on UK adults. Qualitative research is used to gain a holistic, person-centred perspective, and allows researchers to generate detailed accounts that give a dynamic representation of that person's reality (Holloway and Wheeler, 2010). Individual semi-structured interviews permit the examination of social and personal matters in great depth, and can provide researchers with a significant advantage when exploring sensitive subjects (Dicicco-Bloom and Crabtree, 2006, Reid *et al.*, 2005).

Focus groups were also considered as an option. While these would have also allowed for the views and experiences of a number of participants to be considered, due to the public nature of the process there was concern that the researcher would not be able to delve as deeply into each participant's own experiences (Dicicco-Bloom and Crabtree, 2006). Participants may be less confident to voice their own views or disagree with a dominant opinion, and the nature of the group interaction can put pressure on participants to conform to group norms (Acocella, 2012). Due to the potentially sensitive and personal nature of participants' disclosures it was felt that individual semi-structured interviews would capture the potentially complex individual experiences of participants more successfully than a focus group setting.

The choice of telephone over face-to-face interviews was made for a number of reasons. Firstly, telephone interviews were chosen to improve accessibility for all participants who desired to take part. Adults with JHS/EDS-HT have the potential to be a significantly disabled population with restricted mobility; and those with the most severe symptoms could experience difficulty travelling to a location for face-to-face interview. For pragmatic reasons it was not possible for the researcher to visit participants in their own homes. Additionally, compared to the number of participants we would be able to reach by recruiting from the local area, recruitment via telephone allowed for a much more geographically diverse sample to participate.

During the process of NHS ethical approval for Study 2, the Committee questioned the ability of telephone interviews to be as effective in a vulnerable population. Although face-to-face interviews are more commonly employed, telephone interviews have been used successfully to explore other difficult topics with vulnerable groups, such as screening for depression, anxiety and PTSD in pregnant women (Matthey and Ross-Hamid, 2012); interviewing populations at 'high risk' of anxiety disorders (Batelaan *et al.*, 2012), rape survivors (Trier-Bieniek, 2012), and military veterans (Stevelink *et al.*, 2019).

Qualitative telephone interviews have several advantages; they can potentially limit the emotional distress experienced by participants because of the comfort afforded by a less 'exposed' communication method (Trier-Bieniek, 2012). The relative anonymity of the telephone compared to face-to-face interviews has demonstrated that individuals may be more liable to disclose sensitive information

than in a face-to-face interview (Nebot *et al.*, 1994). Studies comparing transcripts of face-to-face to telephone interviews have confirmed both methods to be equally robust in terms of breadth and depth (Sturges and Hanrahan, 2004, Nebot *et al.*, 1994). A disadvantage of this method is the lack of face-to-face interaction. As the interviewer cannot see the interviewee's facial expression or body language, it is not possible to use these as a source of additional information (Mann and Stewart, 2000).

3.5 Patient Research Partner (PRP): Partnership and input

My Patient Research Partner (PRP) for this thesis, Sue Harris, a 60-year-old retired nurse with JHS was recruited early in the study planning stage from the local area to offer additional input and support as a patient with the condition.

Sue had taken part in other JHS-related research and provided honest input through regular face-to-face meetings and additional email contributions at each stage of the planning, implementation and analysis process.

Sue also invited her daughter Claire's input where available, as Claire likewise had JHS and is an active member of a local support group and JHS/EDS helpline. Sue provided input at the initial design phase of the study and provided opinion on all participant information sheets at each stage, to ensure that these were easy to read and understand by the target population. At further points Sue also assisted with feedback regarding the results of the systematic review, and a summary of each study's results, as to whether these resonated with her experiences. Sue and Claire have been much-appreciated and valuable external contributors to this thesis, presenting their understandings and judgments in respect of their own familiarities and knowledge of JHS and its associated conditions. Both provided their consent to being named within this thesis and for their roles to be explicitly (and very gratefully) acknowledged.

3.6 Qualitatively driven methods: A multiphase design

As outlined at the beginning of this section, the primary aims for this thesis are to understand the lived experiences of people with JHS and EDS-HT and to explore psychosocial, cognitive and behavioural impact of these conditions on participants, the results of which will be used to determine recommendations for the components of a behaviour change intervention.

It has been estimated that there are around forty different mixed methods research designs reported within the literature (Tashakkori and Teddlie, 2003). These can include; *convergent parallel designs* (concurrent qualitative and quantitative phases of data collection); *explanatory sequential designs* (where quantitative data and analysis is followed by qualitative data, analysis and interpretation); or *exploratory designs* (qualitative data is built on and informs quantitative interpretation and analysis; (Creswell and Plano Clark, 2018). The current multiphase design goes beyond simple parallel, explanatory or exploratory research designs. At each sequential stage of the multiphase design, qualitative and quantitative phases of data collection build upon the results of what was learned at the prior stage, in order to answer a series of research questions (Creswell and Plano Clark, 2018). Due to the lack of research in the area of JHS/EDS-HT, and in order to ensure that results from both qualitative phases inform the later stage, the decision was made to use a multiphase design, using a sequential strategy (Creswell, 2009). A flowchart outlining each phase of the multiphase design is illustrated below in Figure 4A.

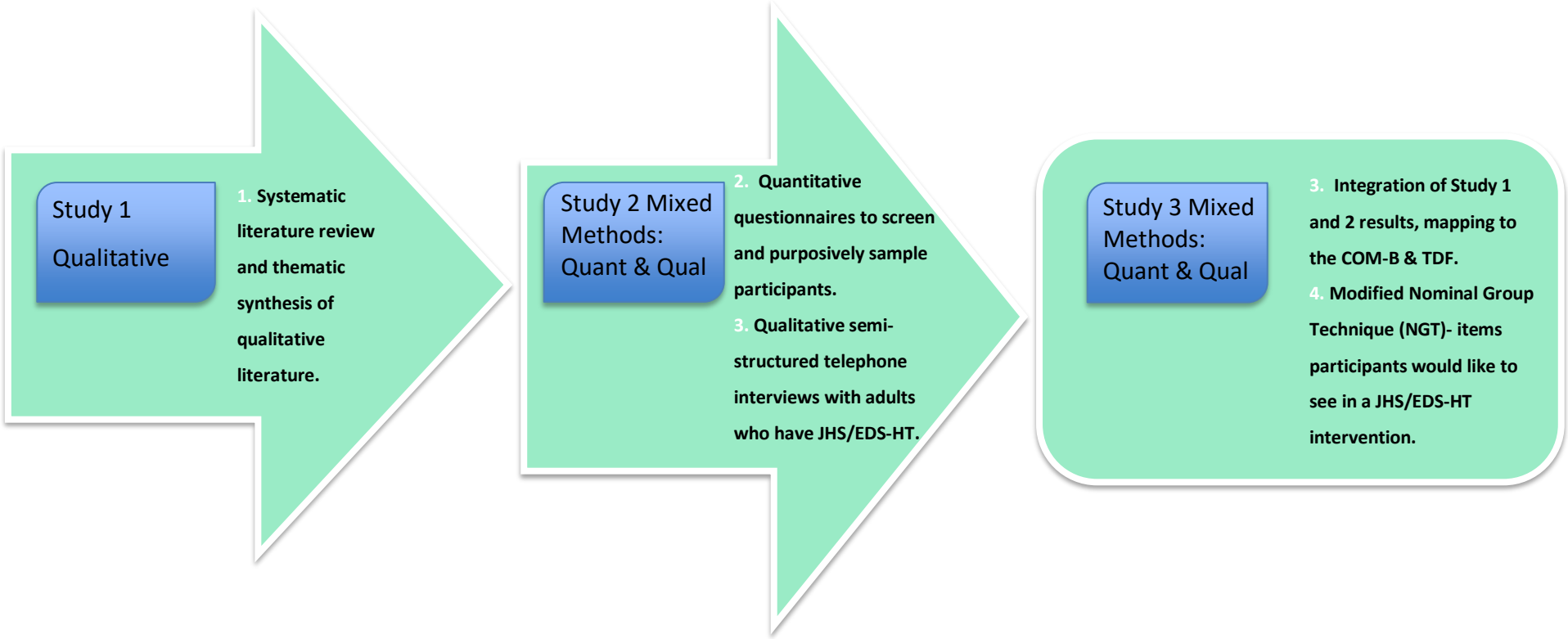
In the present study, firstly qualitative data relating to the lived experiences of those with JHS and EDS was collected and analysed as part of a systematic review (Study 1: Chapter 4). The outcome of this indicated a beneficial opportunity for further qualitative research using a larger number of participants, with exploration of aspects that had not been considered in great depth in previous studies. These results were used to inform questions posed to participants in semi-structured interviews, which examined the psychosocial, cognitive and behavioural impact of JHS/EDS-HT (Study 2). Also in study 2, participant's scores on the Hakim and Grahame 5PQ and the HADS were used to screen for significant anxiety and

depression, and to purposively sample participants for qualitative telephone interviews. The results of these two qualitative phases were combined and used to drive the selection of self-management behaviour change interventions (Study 3).

Nevertheless, there are some limitations to the mixed methods approach. Johnson and Onwuegbuzie (2004) have indicated a number of strengths and limitations of mixed methods. Strengths include the fact that numerical data can be used to add precision to words, pictures and narrative, and can provide stronger evidence for a conclusion through corroboration of the findings (Johnson and Onwuegbuzie, 2004). Limitations include *to the time-consuming nature of the multiphase research design, and potential difficulties carrying out both research approaches efficiently (Creswell and Plano Clark, 2018) . Although the long nature of the sequential studies was noted, due to the structure of the PhD programme, the time-consuming nature was not a major concern at the outset*.

In the present thesis, although quantitative data was incorporated, including using the Hospital Anxiety and Depression Scale (HADS (Zigmond and Snaith, 1983) as a screening tool at Stage 2, and quantitative voting data from Nominal Group Technique (NGT) focus group members considered at Stage 3, these were not analysed using statistics, or developed and triangulated to the same level as qualitative data in each subsequent stage of the study. Participants voting scores were integrated during the interpretation of the findings, and used to prioritise choices for intervention content. The quantitative results are therefore more limited than if a more in-depth quantitative stage had been used, through development of a questionnaire, or use of hypermobility-specific outcome tool such as the Bristol Impact of Hypermobility questionnaire (BIoH, (Palmer *et al.*, 2017, Palmer *et al.*, 2020). Future research could benefit from a greater exploration of quantitative results, considered in partnership with qualitative input from stakeholders with hypermobility, or clinicians with experience treating patients with JHS/EDS-HT.

Figure 3A: The multiphase design and sequential research strategy.



Secondly, issues around mixing each stage of the data have also been noted. Any difficulties noted by the researcher in relation to mixing qualitative and quantitative data in the latter phases of the research are considered in Chapter 6. Lastly, the investigator is required to consider how to translate the research findings into practice through developing materials (Creswell and Plano Clark, 2018). Strengths of this method include the detailed nature of the recommendations, the use of multiple sources of external input during the refinement phases and contribution from patients with JHS/EDS-HT during the prioritisation and discussion of these behaviour change options. This has been considered in greater depth in Chapter 6.

With the use of the multiphase design and sequential strategy, it was hoped that the results generated could contribute to both an understanding of the psychosocial impact of JHS/EDS-HT, and provide the basis for practical recommendations for managing the condition, including future behavioural interventions. In addition, by linking qualitative results to quantitative behaviour change theory, this may give more weight, and possibly be seen as a more practical option to some health services researchers, compared to qualitative data presented alone (Creswell, 2009).

3.7 Critical evaluation of theories relevant to the psychosocial, cognitive and behavioural impact of JHS/EDS-HT

This subsection explores the theoretical basis for this thesis, and presents a critical evaluation of the variety of behavioural models and theories that were considered in the design of this PhD project. Due to the lack of research specifically within JHS/EDS-HT, a range of theoretical models relating to self-management and psychosocial coping in other conditions, including consideration of the wider social and environmental influences on behaviour will be outlined and evaluated. Reasons for the choice of the Theoretical Domains Framework (TDF) and Capability, Opportunity Motivation-Behaviour (COM-B) model for Study 3 are discussed in relevance to adults' experiences of JHS/EDS-HT (Michie *et al.*, 2011). Lastly, the role of these theories in the development of a self-management intervention using the COM-B and TDF combined in the Behaviour Change Wheel will be explored.

As outlined in the previous section this PhD aims to explore adults' lived experiences of JHS/EDS-HT, and the psychosocial, cognitive and behavioural impact. These results will be triangulated to ultimately choose elements of a self-management intervention informed and driven by patients' own experiences and preferences. In this section, by exploring theories relating to common experiences across chronic conditions and the possible interrelating factors in coping and self-management behaviours, the candidate intended to gain a better understanding of how different factors influence participants' perceptions of the psychosocial impact of their condition.

3.7.1 Fear-Avoidance (FA) Model of Chronic Pain

One model that could explain how participants manage their JHS/EDS-HT is the Fear Avoidance (FA) Model, which describes a possible trajectory for patients with acute pain who may be trapped in a circle of pain catastrophising and disability. The FA model was originally proposed by Vlaeyen et al (1995) as a means to explain patients' responses to chronic back pain (Vlaeyen *et al.*, 1995). According to Kori and colleagues (1990), patients in pain may experience an irrational and debilitating fear of injury and movement termed kinesiophobia (Kori K.S. *et al.*, 1990). While the FA model may go some way towards explaining catastrophising and fear of injury in JHS/EDS HT, patients' fear of injury is multifactorial, and a number of studies with patients who have JHS/EDS-HT indicated that patients' fear of injury may also be linked to fears relating to past experiences, such as treatments in hospital (e.g. descriptions of where local anaesthetics had been ineffective, or their symptoms had been misunderstood), rather than a fear of pain and movement itself, which is not taken into account by this model (Berglund *et al.,* 2000; 2010).

In addition, the FA model fails to account for multiple, competing life goals and personal values. For example, people may wish to avoid standing for long periods or leaning over an oven to cook, but may still persevere in spite of pain to cook for friends and family (Crombez *et al.*, 2012). Additionally, people may have the choice between doing an activity that causes pain, or missing out on positive activities such as social interaction. As has been described by Schmidt and

colleagues (2015) participants with JHS/EDS-HT described how they would often 'weigh up', using a cost-benefit analysis, whether a life goal is worth the extra effort, and evaluate the perceived potential consequences (Schmidt *et al.*, 2015). The need to appraise pain avoidance and the potential physical and emotional costs of undertaking the behaviour are not considered by this model, yet are important factors in JHS/EDS-HT.

3.7.2 Health Belief Model

Developed in the early 1950s by social psychologists in the US Public Health Service, the Heath Belief Model (HBM, see Figure 3B below) attempted to conceptualise why people failed to attend preventive screening tests for early detection of disease, and was later adapted to better understand risk-related health behaviour (Janz and Becker, 1984). The HBM developed by Rosenstock (1974, 1988) specifies that if individuals perceive a negative health outcome to be severe, perceive that they are susceptible to that outcome, that the benefits of reducing the likelihood of the outcome is high, and the barriers to adopting preventive behaviours are low, then behaviour is most likely to occur (Rosenstock, 1974, Rosenstock *et al.*, 1988, Carpenter, 2010). For example, if a woman does not believe that she is likely to develop arthritis in old age, then she is unlikely to engage in arthritis preventative behaviours (Miri *et al.*, 2018). In the case of the current research, JHS/EDS-HT patients could assess the perceived threat of their symptoms, as well as the barriers and benefits of accessing medical support or exercise. If a patient with JHS/EDS-HT perceived that their symptoms were more serious or unusual than what they had experienced in the past, they may be driven to seek treatment. If, however they believe that there may be barriers to treatment, such as the belief that treatment would be ineffective (Hope *et al.*, 2017), or that they might not be believed, then they will be less likely to seek support or perform preventative behaviours.

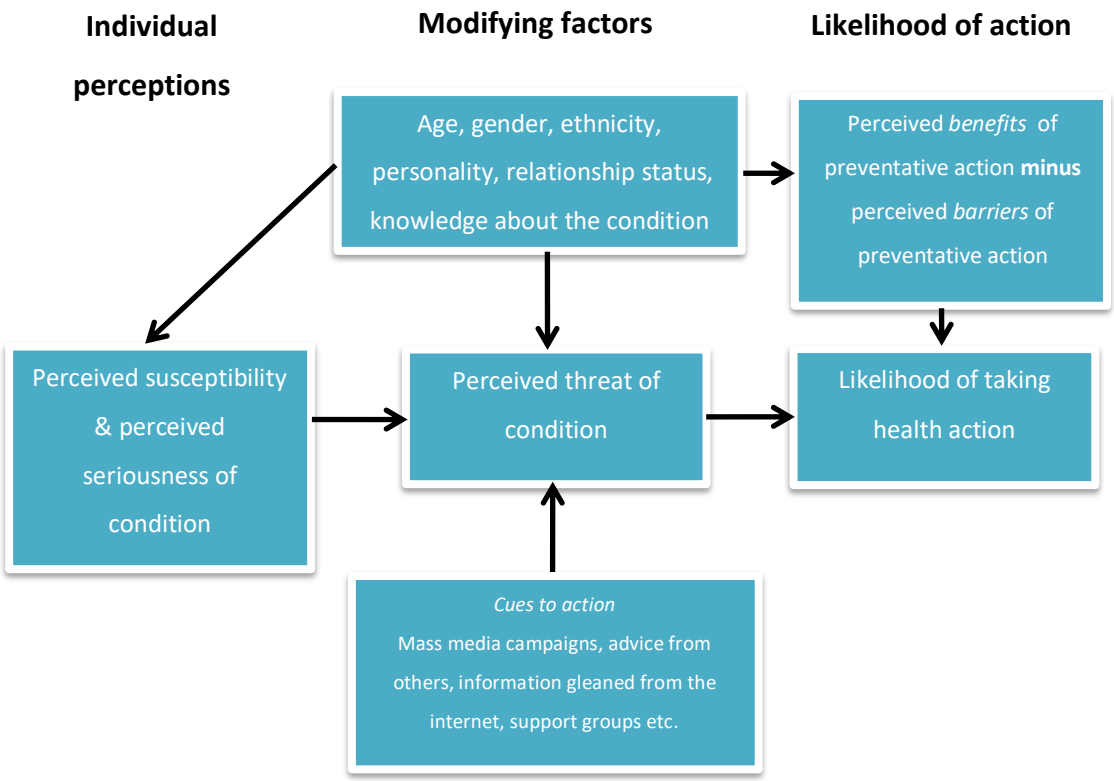


Figure 3B: The Health Belief Model (HBM), adapted from Rosenstock, (1974).

Perceptions of severity of illness are often based on an individual's knowledge of their condition, which is typically gained from disease-specific information sources, such as the internet, social media, and other members of support groups with the same condition. For example, if a person with JHS/EDS-HT gains information about other people with the same condition who have needed medical interventions such as surgery, or whose symptoms have greatly disrupted their life, this individual could potentially perceive any changes in their own symptoms as a more serious threat than if they had not sourced this information.

Conversely, the HBM has been criticised for being overly simplistic. For example, the HBM makes no reference to environmental or social factors, which are often important in people's decisions to seek help and self-manage their condition, such as consulting with family members or friends in deciding whether or not to visit their GP. Secondly, the HBM does not consider emotional influences on behaviour, such as anxiety or anger (Lin *et al.*, 2017). Prior studies have indicated that factors such as anticipatory emotions play an important role in participants' decisions about

HIV screening (Kellerman *et al.*, 2002). For these reasons, a more inclusive model of health behaviour to account for behaviours in JHS/EDS-HT was needed.

3.7.3 The Theoretical Domains Framework

It was recognised from reviewing the literature in Study 1 that quite a broad method would be needed to capture all influences on participants' experience of JHS/EDS-HT. The Theoretical Domains Framework (TDF) was developed by a consensus group of behavioural scientists and stakeholders, in response to criticisms regarding the vast range of behaviour change theories available, and potential overlaps and omissions resulting from the use of one theory over another (Cane *et al.*, 2012). The aim of the TDF framework is to make the assortment of behaviour change theories more accessible to other disciplines, such as public health (Michie *et al.*, 2005a, Cane *et al.*, 2012). The TDF is based on a synthesis of thirty-three theories of behaviour and behaviour change, clustered into firstly twelve (Michie *et al.*, 2005b), and later fourteen domains to create one combined theory of behaviour change (Cane *et al.*, 2012). The TDF's fourteen domains, associated components and definitions include a wide range of factors that are likely to influence participant behaviour change, and are illustrated in Table 3.1 below. Furthermore, the TDF domains can also be mapped to each component in the behaviour change wheel (BCW), and this is further explained below.

Table 3.1 The fourteen TDF domain definitions, with their 84 associated TDF component constructs and equivalent COM-B model construct (adapted from Cane *et al.* 2012 and Michie *et al.* 2014 p. 88-91).

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Knowledge	Knowledge (including knowledge of a condition/scientific rationale)	An awareness of the existence of an entity or concept, e.g. knowledge of health condition.	**Capability**	**Psychological capability**
	Procedural knowledge			
	Knowledge of task environment			
Memory, attention and decision processes	Memory	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives, e.g. decision-making.		
	Attention			
	Attention control			
	Decision-making			
	Cognitive overload/tiredness			
Behavioural regulation	Self-monitoring	Anything aimed at managing or changing objectively observed or measured actions, e.g. self-monitoring.		
	Breaking habit			
	Action planning			

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Skills	Skills	An ability or proficiency acquired through practice, e.g. interpersonal skills.	**Capability**	**Physical capability**
	Skills development			
	Competence			
	Ability			
	Interpersonal skills			

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Social/professional role and identity	Professional identity	A set of behaviours and displayed personal qualities of an individual in a social work setting, e.g. social or professional identity.	**Motivation**	**Reflective motivation**
	Professional role			
	Social identity			
	Identity			
	Professional boundaries			
	Professional confidence			
	Group identity			
	Leadership			
	Organisational commitment			
Beliefs about capabilities	Self-confidence	Acceptance of the truth, reality or validity about an ability, talent of facility that a person can put to constructive use, e.g. self-efficacy.		
	Perceived competence			
	Self-efficacy			
	Perceived behavioural control			
	Beliefs			
	Self esteem			
	Empowerment			
	Professional confidence			
	Action planning			
	Implementation intention			

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Optimism	Optimism	The confidence that things will happen for the best, or that desired goals will be attained, e.g. unrealistic optimism.	**Motivation**	**Reflective motivation**
	Pessimism			
	Unrealistic optimism			
	Identity			
Beliefs about consequences	Beliefs	Acceptance of the truth, reality or validity about outcomes of the behaviour in a given situation e.g. outcome expectancies.		
	Outcome expectations			
	Characteristics of outcome expectations			
	Anticipated regret			
	Consequences			
Intentions	Stability of intentions	A conscious decision to perform behaviour or resolve to act in a certain way, e.g. stability of intentions.		
	Stages-of-change model			
	Transtheoretical model and stages-of-change model			
Goals	Goals (distal/proximal)	Mental representations of outcomes or end states an individual wants to achieve, e.g. action planning.		
	Goal priority			
	Goal/target setting			
	Goals (autonomous/controlled)			
	Action planning			
	Implementation intention			

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Reinforcement	Rewards (proximal/distal, valued/not valued, probable/improbable)	Increasing the probability of a response by arranging a dependent relationship, for contingency, between the response and a given stimulus, e.g. incentives.	**Motivation**	**Automatic motivation**
	Incentives			
	Punishment			
	Consequences			
	Reinforcement			
	Contingencies			
	Sanctions			
Emotions	Fear	A complex reaction pattern involving experiential, behaviour and psychological elements, by which the individual attempts to deal with a personally significant matter or event, e.g. fear.		
	Anxiety			
	Affect			
	Stress			
	Depression			
	Positive/negative affect			
	Burnout			

TDF Domain	TDF Construct	TDF domain definition	Matching COM-B model construct	
Environmental context and resources	Environmental stressors Resources/material resources Organisational culture/climate Salient events/critical incidents Interaction of person and environment Barriers and facilitators	Any circumstance of a person's situation or environment that discourages or encourages development of skills and abilities, independence, social competence, and adaptive behaviour e.g. resources/material resources.	**Opportunity**	**Physical opportunity**
Social influences	Social pressure Social norms Group conformity Social comparisons Group norms Social supports Power Intergroup conflict Alienation Group identity Modeling	Interpersonal processes that can cause individuals to change their thoughts, feelings, and behaviours e.g. social norms.		**Social opportunity**

3.7.4 The COM-B Model (Michie et al., 2011)

The capability, opportunity, motivation-behaviour (COM-B) model was developed and designed as a complementary partner to the TDF, as each of the TDF constructs correlates with the applicable COM-B construct. Michie and colleagues built upon the prior success of the Theoretical Domains Framework (Michie *et al.*, 2005b), noting that the nature of behaviour had remained under-theorised when developing behaviour change interventions (Michie *et al.*, 2011). Therefore, in order to choose which interventions would be most effective, the authors suggested starting with a model of behaviour. The model not only focuses on the external environment, but also captures a range of internal factors that may be involved in behaviour change, such as psychological and physical mechanisms (Michie *et al.*, 2011).

The COM-B model suggests that three main factors drive positive health behaviours (B): capability (C), opportunity (O), and motivation (M) to engage in the behaviour. Behaviour change interventions can be defined as '*co-ordinated sets of activities designed to change specified behaviour patterns*' (Michie *et al.,* 2011 p.1, see Figure 3C). In order for the desired behaviour to occur, the COM-B model indicates that each person must have the three factors. 'Capability' can be defined as the physical or psychological capacity of a person to engage in the activity, including the required knowledge and skills. 'Opportunity' refers to the factors external to the individual that can enable or prompt the behaviour. 'Motivation' signifies the brain processes that encourage and direct behaviour, including habits, emotional responses and decision-making (Michie *et al.*, 2011).

The arrows in Figure 3C represent how each of the components within the COM-B model could influence each other; for example, any change in a participant's behaviour will involve the interaction of capability, opportunity and motivation components. The bidirectional arrows indicate that capability, opportunity, and motivation can also, therefore, influence behaviour. Likewise, capability and opportunity can change motivation (Michie *et al.,* 2011).

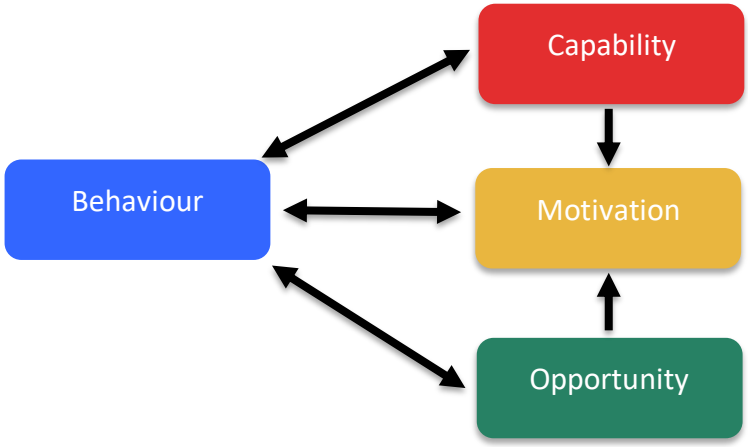


Figure 3C: The Capability, Opportunity, Motivation-Behaviour (COM-B) model, adapted from Michie *et al.,* 2011.

However, Michie and colleagues (2011) noted a number of important distinctions within the literature that needed to be taken into account when considering the three COM-B factors. In order to address these, six subdivisions were proposed (see table 3.1), two for each factor:

3.7.4.1 Capability: Physical and Psychological

Physical capability (the ability to undertake the behaviour) can be distinguished from psychological capability (the capacity to engage in the necessary thought processes, such as reasoning or comprehension). As illustrated in Table 3.1, the TDF constructs *knowledge*, *skills*, *memory, attention and decision processes, behaviour regulation* and *physical skills* map onto the capability construct of the COM-B model. From the perspective of managing JHS/EDS-HT, knowledge could refer to a lack of understanding about the condition, (from healthcare professionals or the general public) or misinterpretation of symptoms by the patient themselves (Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016, Schmidt *et al.*, 2015). Skills may refer to participants' abilities to perform household tasks or to fulfil demands, such as breaking activities down into smaller steps to make them easier to achieve (Schmidt *et al.*, 2015, Palmer *et al.*, 2016b).

3.7.4.2 Opportunity: Physical and Social

Opportunity can be further distinguished between physical opportunity (afforded by the physical environment) and social opportunity (afforded by culture and society; Michie *et al.,* 2011). Under the opportunity construct of the COM-B, the TDF constructs; *social influences* and *environmental contexts and resources* are included. In relation to the JHS/EDS-HT literature, this could relate to the fluctuating nature of people's symptoms, as they struggle to be independent and to interact with their environment due to barriers, such as terrain or accessibility, or fluctuating physical symptoms (De Baets *et al.*, 2017). Because of symptom variability, with participants feeling better on some days than others, it was hard for them to plan ahead, and their activities could be very limited on days when they were in pain (Berglund *et al.*, 2000, Schmidt *et al.*, 2015). Social opportunity also refers to the social comparisons that participants make between themselves and others (Schmidt *et al.*, 2015, Terry *et al.*, 2015).

3.7.4.3 Motivation: Reflective and Automatic

Participants must have sufficiently strong *motivation* to complete the target behaviour without being distracted by competing alternative behaviours; this motivation can be reflective (self-conscious planning, intentions, evaluations) or automatic (reflex responses, impulses). The TDF constructs; *reinforcement, emotions, social/professional role and identity, beliefs about capabilities, beliefs about consequences, goals* and *intentions* match to the motivation construct of the COM-B. In the context of the literature, for people with JHS/EDS-HT these may refer to beliefs about pregnancy and the perceived consequences of having children (Berglund *et al.*, 2000, De Baets *et al.*, 2017). Alternatively, beliefs relating to exercise and physiotherapy would fall under this theme (Palmer *et al.*, 2016b). Emotions could refer to feelings of fear, whether fear of potential injury (Lumley *et al.*, 1994, Schmidt *et al.*, 2015, Terry *et al.*, 2015), fears relating to hospital treatment

(Berglund *et al.*, 2000), guilt and shame relating to depending on family members for support, or having to give up activities due to pain (Schmidt *et al.*, 2015).

3.7.5 Use of the COM-B in published research

The National Institute for Health and Clinical Excellence (NICE) recommends COM-B for cost-effective behaviour change interventions at an individual level (National Institute for Health and Care Excellence, 2014a). Although a relatively new method, the COM-B model has been used successfully to improve hearing aid use in adults (Barker *et al.*, 2016), identify barriers to chlamydia testing (Mcdonagh *et al.*, 2017), improve medication adherence (Easthall and Barnett, 2017), in an exercise intervention for osteoarthritis (Hurley *et al.*, 2016), in a physical activity intervention to manage rheumatoid arthritis fatigue (Salmon *et al.*, 2019) and to promote overall health for young people with high psychosis risk (Carney *et al.*, 2016). While the TDF and COM-B have yet to be applied within the setting of managing the psychosocial impact of JHS/EDS-HT, it is clear from the literature that both individual and broader external psychosocial and environmental factors affect participants' abilities to cope with and self-manage their condition. An advantage of this model over those considered at earlier stages of this work is that the COM-B and TDF take into account potential social influences on behaviour, such as social comparisons to others and the availability of social support to patients. The TDF and COM-B also take into account patients' interpretations of the severity of their condition, as well as perceived consequences of certain actions, such as becoming pregnant.

3.7.6 The Behaviour Change Wheel (BCW)

So far, we have explored how the TDF and its associated constructs map onto the six components within the COM-B behavioural system. The BCW was chosen for the present thesis as it has a number of advantages. For example, it is designed to provide a systematic framework to identify a number of sources for each behaviour, including internal, external, automatic and chosen behaviours. This analysis of determinates of behaviour enables researchers to define what needs to change in

order for the unwanted behaviour to stop, or for the desired behaviour to occur (Barker *et al.*, 2016). Secondly, once an understanding of the behaviour to be changed has been identified, the BCW provides a starting point for researchers to systematically identify intervention functions (See Table 3.2), and later potential policy categories that could facilitate behaviour change.

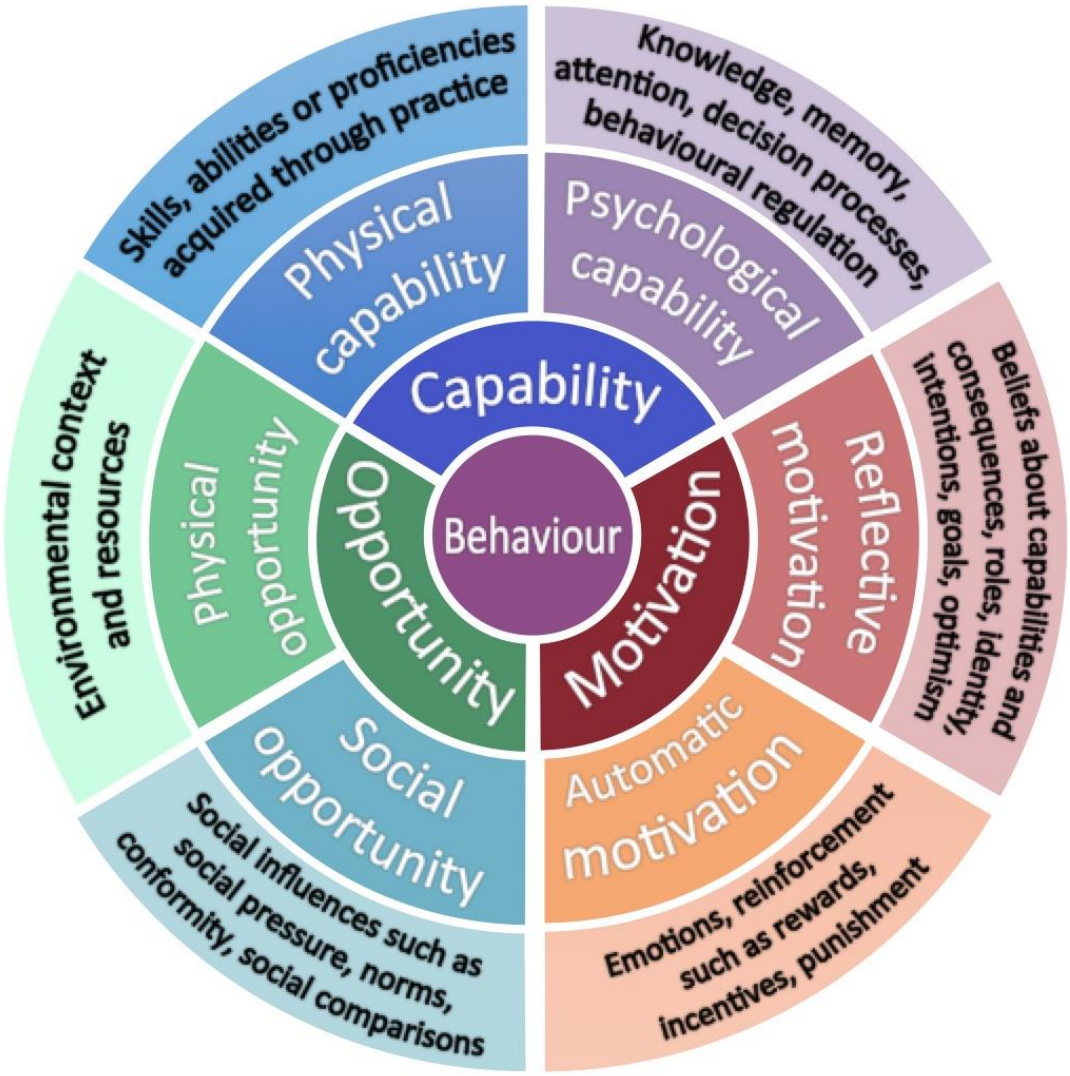


Figure 2D: The Behaviour Change Wheel (BCW; adapted from Michie *et al*., 2011). The Capability, Opportunity, Motivation, Behaviour (COM-B) model sits at the centre of the BCW. The COM-B (white text, inner rings) fits into the Theoretical Domains Framework (TDF; black text outer ring; Michie *et al.,* 2011).

Table 3.2: Definitions of BCW interventions adapted from Michie et al., 2011.

Intervention	Definition	Examples
Education	Increasing knowledge or understanding	Providing information to promote healthy eating
Persuasion	Using communication to induce positive or negative feelings or stimulate action	Using imagery to motivate increases in physical activity
Incentivisation	Creating expectation of reward	Using prizes to induce attempts to stop smoking
Coercion	Creating expectation of punishment or cost	Raising the financial cost to reduce excessive alcohol consumption
Training	Imparting skills	Advanced driver training to increase safe driving
Restriction	Using rules to reduce the opportunity to engage in the target behaviour (or reduce the opportunity to engage in competing behaviours)	Prohibiting sales of solvents to people under 18 to reduce use for intoxication
Environmental restructuring	Changing the physical or social context	Providing on-screen prompts for GPs to ask about smoking behaviour
Modeling	Providing an example for people to aspire to or imitate	Using TV drama scenes involving safe-sex practices to increase condom use
Enablement	Increasing means or reducing barriers to increased capability or opportunity	Behavioural support for smoking cessation, surgery to reduce obesity

In the management of other chronic pain conditions, such as osteoarthritis, individualised self-management strategies are used as an effective means of implementing positive behaviour change activities such as physical activity and exercise (National Institute for Health and Care Excellence, 2014b). However, to date no research has examined the benefits of a behaviour change intervention in the JHS/EDS-HT population. Such an intervention needs to be based on robust behaviour

change theory, and ideally informed by contributions from patients with JHS/EDS-HT, and the healthcare professionals involved in their care.

3.8 Justification for choosing the modified Nominal Group Technique (NGT), compared to other potential decision-making group consensus methods

The third study within of this thesis utilised a modified Nominal Group Technique (NGT) focus group method, in order to gain group consensus regarding a variety of self-management behaviour change interventions. Focus groups have the useful advantage for a researcher of being able to gain the views of a large number of participants at once, through natural, spontaneous input and responses. Yet, focus groups do have the potential to be biased by group influences or group effects, particularly if more strongly–willed participants are keen to get their points across. The views and opinions of quieter members of the group may then not be heard as prominently, or at all.

3.8.1 Delphi Technique

In order to gain a fairer, balanced input and group agreement from members, there were several consensus techniques available. One of these was a Delphi technique, a consensus method that allows for group interactions via questionnaires rather than face-to-face discussions. The Delphi Technique was developed in 1953 by the Rand Corporation as a tool to gain opinions from groups of experts (Donohoe *et al.*, 2012) and uses a series of staged quantitative questionnaires with individual feedback to each participant (Mcmillan *et al.*, 2016). Through all stages each participant is asked to rank their responses and then reconsider their positions in light of group trends (displayed to participants as the average response of the other participants) until opinions converge to a consensus, usually after the third or fourth round of questionnaires (Donohoe *et al.*, 2012, Novakowski and Wellar, 2008).

The advantages of this method are the relative anonymity compared to other methods, the lack of need for participants to be in close proximity to each other and the opportunity for participants to provide an equal response to items (Donohoe and

Needham, 2009, Novakowski and Wellar, 2008). Nonetheless, there are some disadvantages of the Delphi Technique, the most important being the risk of group conformity. On being told that the average vote has centred around one area of a Likert scale, participants may feel social pressure to change their judgements in order to 'fit in' with the majority. This phenomenon is termed 'normative social influence', and in order to avoid negative consequences such as social disapproval, or in situations in which the correct response is unclear, people will often look to others as a source of information on which to base their decisions (Bolger and Wright, 2011). The Delphi Technique can also be time-consuming, relatively labour-intensive for participants having to repeat surveys, and as a result there is a noted risk of participant attrition over time (Keeney *et al.*, 2011, Donohoe and Needham, 2009). For the purposes of the present study, we were keen to hear participants' reasoning behind their decisions. In addition, repeated communication via post or email written methods may have been more challenging to some patients with chronic illness than communicating their ideas in a one-time event.

3.8.2 Q-Methodology

A second option was Q-Methodology. This is a method that is also concerned with the individual viewpoint of participants and involves providing participants with a set of items (called the Q-Sample) which contributors then rank in a strategic process according to how much they agree or disagree with the items (known as a Q-Sort; (Dziopa and Ahern, 2011). Its advantages include the formation of the opinion statements for the Q-Sample involving input from a wide range of data on the topic under scrutiny, including semi-structured interview, focus group and journal article data in a 'concourse' (Amin, 2000, Dziopa and Ahern, 2011). This was seen to be an advantage for the current study as in this case the input of a wide variety of data relating to the views and lived experiences of JHS and EDS-HT were considered. Q-Methodology also had the advantages of participant anonymity during the voting process, the chance to work with participants in a face-to-face setting and featured the opportunity for participants to rank pre-determined statements, which would fit

well with our plans to present participants with various behaviour change options for JHS/EDS-HT.

However, the Q-Methodology method was deemed to be too time-consuming for the present study, as each participant would have to be visited individually and the Q-Sort process completed face-to-face over several hours. In addition, this technique did not feature the chance for participants to discuss the reasoning for their choices, or to explore shared experiences or have input from others with JHS/EDS-HT at any point during the process, something that was deemed a significant consideration for the selected method.

3.8.3 Nominal Group Technique (NGT)

A third option was Nominal Group Technique (NGT), a method in which participants in a group setting are invited to rank and re-rank items, which is followed by active group discussion and a second ranking of items. The NGT method has a number of advantages over the Q-Sort and Delphi Techniques. Firstly, the NGT method is open to modification, a useful option in the present study as unlike the traditional NGT method (in which participants devise solutions to a proposed question using a round-robin method), these solutions had already been identified via the COM-B and TDF mapping process. In the case of the present research, it was participants' individual ranking and preferences for items that were deemed most important.

Although the NGT has potential limitations, through careful consideration of participant input methods we were able to moderate the influence of these shortcomings. Firstly, a potential disadvantage is that anonymous participant responses via the voting process are not always possible, and participants risk conformity to the majority, as identified in the Delphi Technique. In order to control for group conformity, participants were given the option to vote individually and anonymously using Audience Response System (ARS) Turningpoint ResponseCard keypads, which gave anonymised data responses for each question. Secondly, participants could not see the scores of the other group members until *after* the

question had been answered, thereby removing any chance of participant conformity bias due to the choices of other group members.

A further potential limitation of the NGT method is that the researcher decides the cut-off score for group consensus. In order to counteract any potential bias, the degree of conformity for an affirmative group consensus was decided in advance of data collection, in consultation with a member of the research team (NW), in order to ensure the validity of the data.

3.9 Conclusion

In conclusion, this chapter has examined the use of mixed methods in health research, and the need to involve participants with JHS/EDS-HT and a PRP as true partners in the research process. The potential influence of the PhD candidate's own history and the influence of power imbalances in qualitative research, and how these were minimised or eliminated through use of reflexivity were considered. Next, this chapter examined the range of processes put in place by the candidate to ensure rigour, such as the CASP (Study 1) and COREQ (Study 2) checklists. The methods employed to reach hard-to-reach communities such as patients with JHS/EDS-HT were outlined, including networking with patient support groups. Theories relevant to the psychosocial, cognitive and behavioural impact of JHS/EDS-HT were summarised and critically evaluated. Lastly, justification for the use of the Nominal Group Technique was given, and compared to other alternatives such as the Delphi technique or Q-Methodology. As discussed, this thesis has used a multiphase mixed methods design. The final methodological choices for this study include the use of internet-based recruitment via social media (Study 2 and 3) and telephone interviews to conduct semi-structured interviews (Study 2) to ensure as broad a geographical range of participants as possible. Lastly, the barriers to effective management of JHS/EDS-HT were mapped to the COM-B and TDF (Study 3) and participants with JHS/EDS-HT invited for face-to-face individual voting and group discussion regarding their preferred options for a self-management intervention for JHS/EDS-HT. These methods were chosen as the best options in order to gain

valuable input from a range of participants, using methods and methodology considerate of their needs.

4 Chapter 4, Study 1: The lived experience of Joint Hypermobility and Ehlers-Danlos Syndromes: A systematic review and thematic synthesis.

This chapter gives an overview of the lived experiences of adults with JHS/EDS-HT, through a systematic review of published qualitative literature. An edited version of this chapter was published in the journal Physical Therapy Reviews in April 2019:

> Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. 2019, "The lived experience of Joint Hypermobility and Ehlers-Danlos Syndromes: a systematic review and thematic synthesis", *Physical Therapy Reviews*, vol. 24, no. 1-2, pp. 12-28. https://doi.org/10.1080/10833196.2019.1590674

4.1 Introduction

As discussed in Chapter 2 of this thesis, recent systematic reviews have found that those with JHS suffered significantly greater psychological distress compared to those without the condition, namely anxiety, depression and panic disorders (Sanches *et al.*, 2012, Smith *et al.*, 2014b). The multifactorial impact of JHS and EDS can lead to poor health-related quality of life (Anderson *et al.*, 2014), and restricted physical and psychological functioning (Maeland *et al.*, 2011). A lack of professional awareness of the syndromes can cause considerable delay in diagnosis, and the otherwise normal outward appearance of patients can lead healthcare professionals to question the legitimacy of their pain and symptoms (Berglund *et al.*, 2010).

While it is clear that people with JHS and EDS may experience significant anxiety, depression and psychological distress, a comprehensive understanding of the lived experiences of those with the conditions is lacking. There has yet to be a systematic review examining the qualitative data produced by participants themselves; their own lived experiences. Thematic synthesis has been used effectively in other systematic reviews that examine qualitative patient experiences

and perspectives (Boehmer *et al.*, 2016, Morton *et al.*, 2010, Thomas and Harden, 2008). The method uses rigorous and explicit methods to combine the results of primary research studies, aiming to develop analytical themes and an interrelated theoretical framework that explains perspectives and experiences (Boehmer *et al.*, 2016, Morton *et al.*, 2010, Thomas and Harden, 2008). Therefore, the purpose of this systematic review is to understand the lived experiences of people with JHS and EDS using thematic synthesis; the first aim of this thesis

4.2 Materials and Methods

4.2.1 Information Sources

Eight online databases were searched (AMED, CINAHL, EMBASE, MEDLINE, PubMed, PsychINFO, SPORTDiscus and the Cochrane Library) from January 1990 (to safeguard the currency of information and diagnostic criteria), to February 2018. The Open Grey database was also searched for unpublished literature. The search strategy is available in the Table 4.1 below. Authors of included papers were contacted where possible to ensure that no relevant papers were due to be published imminently, but none had any additional data to offer. Papers were limited to those written in English, featuring qualitative methodology, or mixed methodology with qualitative data reported independently. Qualitative methods were sought as they were most likely to feature description of peoples' lived experiences of JHS/EDS in their own words.

Table 4.1: Search Strategy: Items from each concept were combined together using "OR" operatives. Items from Concept 1 and Concept 2 were combined within the search strategy using "AND".

Key search concept 1: Hypermobility Syndromes	Key Search Concept 2: Lived Experience
Hypermobility	personal reflection
Joint Hypermobility	lived experience
Ehlers-Danlos	qualitative
	focus group
	phenomenology
	personal experience
	interview

4.2.2 Study Selection & Data Extraction

A process described by Dundar and Fleeman (Dundar and Fleeman, 2017) was used to refine the results of identified papers, based on screening the title and abstract and then the full text using the eligibility criteria. Any duplicates were removed. Papers that did not meet the criteria were excluded. The reasons for exclusion included a study of lived experience that only examined quantitative data (Murray *et al.*, 2013), interviews examining parents experiences where JHS was not assessed (Birt *et al.*, 2014). Excluded papers also included mixed focus groups with adults and children who had EDS, however it was unclear which quotes were from adults, and which from children (Lumley *et al.*, 1994). Lastly, one questionnaire did not report qualitative data alone (Palmer *et al.*, 2017). Descriptive data regarding the sampling procedure, participants, data collection method, data analysis method, major and minor themes were extracted.

4.2.3 Eligibility Criteria

Identified papers had to meet the following eligibility criteria to be included in the review: 1) People with a diagnosis of either Joint Hypermobility Syndrome or Ehlers-Danlos Syndrome, and clearly distinguished from generalised joint hypermobility (hypermobility that is not associated with pain); 2) Papers featuring qualitative methodology, or mixed qualitative and quantitative methodology with qualitative data reported independently; and 3) Papers published in English. While we originally intended to focus on studies that had recruited adults with JHS and EDS-HT only, two key papers recruited participants across all subtypes of EDS (Berglund *et al.*, 2000, Berglund *et al.*, 2010, De Baets *et al.*, 2017). Therefore the inclusion criteria were broadened to include participants of all ages with all EDS subtypes.

4.2.4 Quality Assessment

Two authors (SB, SP) independently reviewed all the full text articles included in the study for quality using the Critical Appraisal Skills Programme (CASP) checklist for qualitative research (see Table 4.3, (Critical Appraisal Skills Programme, 2016). The ten-item CASP tool assesses methodological quality by asking the reviewer to systematically consider a range of potential areas (e.g. "Was a qualitative methodology appropriate?"), and rate each as "yes", "no", or "can't tell" (in cases where more information is required, (Critical Appraisal Skills Programme, 2016). To appraise the overall methodological quality, each study was assigned a numeric quality value based on their CASP score (Chenail, 2011), where 'yes'= 1 point, 'can't tell'= 0 points, 'no'= -1 points, up to a maximum of 10 points:

- Low quality= 0-3
- Medium quality= 4-7
- High quality= 8-10

These were assigned in a table using colour-coding (low; red, medium; orange and high quality; green) for each of the CASP categories, and an overall score produced (see Table 4.3 below). Any differences were resolved through discussion between the two authors (SB, SP) to reach consensus, in accordance with current

Centre for Reviews and Dissemination guidance (University of York. Centre For and Dissemination, 2009)

4.2.5 Thematic Synthesis

The results sections and any additional qualitative data files (Palmer *et al.*, 2016b) from each of the identified final papers were imported verbatim into NVivo 10 (QSR International, Melbourne, Australia), as recommended by Thomas and Harden (Thomas and Harden, 2008). Where opinions of both healthcare professionals and patients had been sought (Palmer *et al.*, 2016b), only data relating to participants with JHS/EDS were coded. Thematic synthesis involved three stages: free line-by-line coding of the findings of primary papers; the organisation of free codes into related areas to construct 'descriptive' themes; and the development of analytical themes representative of participants' perspectives and experiences of JHS and EDS (Thomas and Harden, 2008). The first author, SB, conducted the thematic synthesis, the results of which were reviewed and discussed with the other authors. A Patient Research Partner with JHS (SH) was consulted to ensure the primary thematic synthesis was relevant to the experiences of those with the condition.

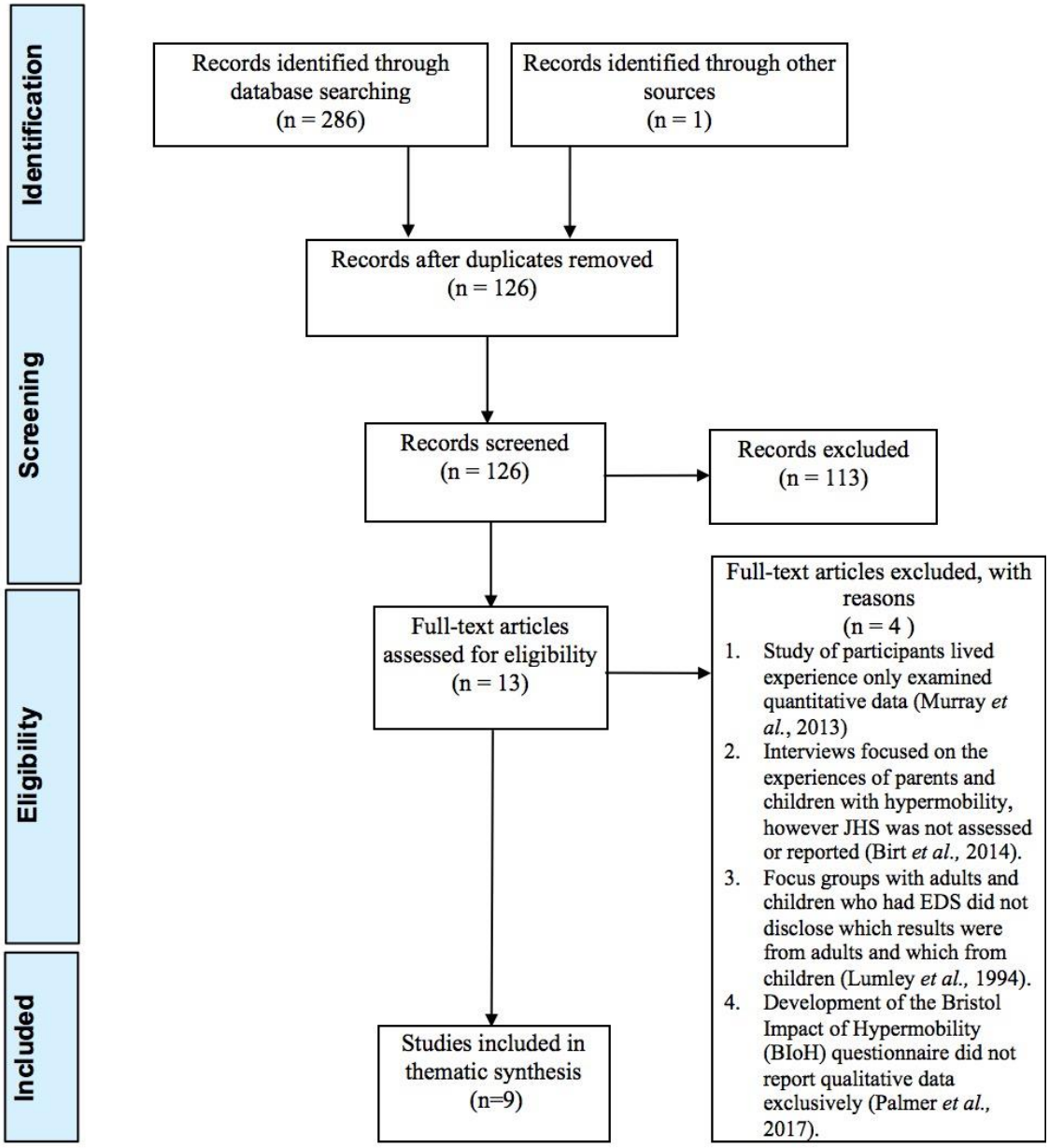


Figure 4A: Flow diagram of study selection, following PRISMA guidelines (Moher *et al.,* 2019).

4.3 Results

4.3.1 Included Papers

The screening process for the selection of suitable articles is detailed in Figure 4A.

4.3.2 Study Characteristics

The majority of included papers had been published within the last 3 years (six of the nine, see Table 4.2). Papers were conducted in the United Kingdom (Palmer *et al.*, 2016b, Palmer *et al.*, 2016a, Schmidt *et al.*, 2015, Simmonds *et al.*, 2016, Terry *et al.*, 2015), United States (Berglund *et al*., 2010, Bovet *et al*., 2016), Belgium (De Baets *et al*., 2017) and Sweden (Berglund *et al.*, 2000). Four papers used clinically confirmed diagnosis (De Baets *et al.*, 2017, Palmer *et al.*, 2016a, Palmer *et al.*, 2016b, Terry *et al.*, 2015); all others relied upon self-reported diagnosis. Four of the included papers used focus groups (Bovet *et al.*, 2016, Palmer *et al.*, 2016b, Terry *et al.*, 2015), three used interviews (Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015) and two used written questionnaire methods to gain feedback (Berglund *et al.*, 2010, Simmonds *et al.*, 2017).

4.3.3 Methodological Appraisal

The aims of the included papers were to describe peoples' experiences (Berglund *et al.*, 2010, Palmer *et al.*, 2016a), lived experiences (Terry *et al.*, 2015), perceptions of daily life with EDS (Berglund *et al.*, 2000), lived experiences concerning diagnosis, daily life with EDS-HT and becoming a mother (De Baets *et al.*, 2017), decisions about activity (Schmidt *et al.*, 2015), views of physiotherapy (Palmer *et al.*, 2016b) and experiences of physiotherapy (Bovet *et al.*, 2016, Simmonds *et al.*, 2017, Simmonds *et al.*, 2016).

Three of the included papers were associated with a randomized controlled trial (RCT) of physiotherapy for adults with JHS (Palmer *et al.*, 2016a). Two of the three papers (Palmer *et al.*, 2016b, Terry *et al.*, 2015) were based on the same focus group data (n= 25; 22 women, 3 men) but with the output analysed from two different perspectives; participants' views of physiotherapy (Palmer *et al.*, 2016b) and their lived experiences of JHS (Terry *et al.*, 2015). Therefore, as these analytical perspectives were different, data from both papers were extracted for the thematic synthesis.

The appropriateness of each study was judged on the clarity and accuracy of reporting against the CASP tool, in addition to a holistic judgement of each study's

ability to contribute first-hand knowledge and understanding of participants' experiences and perceptions of JHS/EDS.

A common recruitment source was from a JHS/EDS support group (Bovet *et al.*, 2016), such as the Ehlers-Danlos National Foundation (EDNF) (Berglund *et al.*, 2010), Flemish Association for Ehlers-Danlos Syndrome (De Baets *et al.*, 2017), Hypermobility Syndromes Association (HMSA; (Terry *et al.*, 2015, Palmer *et al.*, 2016b, Simmonds *et al.*, 2017), Ehlers-Danlos Support UK (EDS-UK; (Simmonds *et al.*, 2016) or from EDS conferences (Berglund *et al.*, 2000). Other sources included a pain management clinic (Schmidt *et al.*, 2015), medical genetics clinic (Bovet *et al.*, 2016) and physiotherapy services (Bovet *et al.*, 2016, Terry *et al.*, 2015, Palmer *et al.*, 2016b, Palmer *et al.*, 2016a).

The results and associated criteria for the CASP-based critical appraisal are summarised in Table 4.3. Overall, the majority of papers had high methodological quality and findings were clearly presented. High quality papers gave a detailed account of the qualitative design and analysis methods used. There was a general lack of clarity regarding the relationship between participants and researchers; only four papers considered bias during formation of the research questions, recruiting research partners with JHS/EDS to provide feedback on questions and the study design (De Baets *et al.*, 2017, Palmer *et al.*, 2016b, Simmonds *et al.*, 2017, Terry *et al.*, 2015).

Table 4.2: Methodological details and themes of included papers.

Authors	Location	Diagnosis	Sample size (n), sex and age	Sampling procedure	Data collection	Themes identified
(Berglund *et al.*, 2000)	Sweden	EDS (subtypes not specified)	11: 7 women, 4 men (mean age not stated, range 21- 67)	Opportunity sample of Swedish EDS support group members	Interviews, Grounded theory	Main theme= Living a restricted life, captured the essence of what it means to have EDS. Subthemes= 1) Living with fear; 2) Living with pain; 3) Feeling stigmatized; 4) Experiences of non-affirmation in healthcare; and 5) Limited self-actualization.
(Berglund *et al.*, 2010)	United States	EDS (subtypes not specified)	22: Sex not stated (mean age 43.5 yrs, range 23-73)	Opportunity sample of EDS support group members (EDNF).	Narrative form, Content analysis	1) Being ignored and belittled by healthcare professionals; 2) Being assigned psychological and/or psychiatric symptoms; 3) Being treated and considered merely as an object; 4) Being trespassed in one's personal sphere; and 5) Being suspected of family violence (child abuse).
(Bovet *et al.*, 2016)	United States	JHS/EDS-HT	13: 9 women, 3 men (mean age 40.5 yrs, range 28 - 57)	Opportunity sample from a medical genetics clinic, a local patient support group, and a physiotherapy program.	Focus groups, framework approach	1) Factors leading to iatrogenic injuries; 2) Other factors contributing to poor-quality care; 3) Contributors to high-quality care; and 4) Provider knowledge of EDS-HT/JHS.

Authors	Location	Diagnosis	Sample size (n), sex and age	Sampling procedure	Data collection	Themes identified
(De Baets *et al.*, 2017)	Belgium	EDS-HT	10: all women (mean age 40.4 yrs, range 31-56)	Purposive sample of participants from a Flemish EDS support group.	In-depth interviews, PH	1) Getting a diagnosis is a relief and supports the choice to become a mother; 2) EDS-HT causes emotional distress, imposes a physical burden and has a major impact on social behaviour; 3) EDS-HT demands a restructuring of everyday activities; 4) Children's and mothers' expectations do not correspond; 5) Having a supportive social and physical environment is of major importance; and 6) The presence of the child reduces the feeling of illness of the mother.
(Palmer *et al.*, 2016a)	United Kingdom	JHS	25: 22 women, 3 men (mean age 33 yrs, range 19 – 60)	Purposive sample of NHS physiotherapy patients and UK support group members (HMSA).	Focus groups, constant comparison	1) JHS as a difficult to diagnose, chronic condition; 2) Physiotherapy to treat JHS and 3) Optimizing physiotherapy as an intervention for JHS.
(Palmer *et al.*, 2016b)	United Kingdom	JHS	18: 15 women, 3 men (mean age 36.5 yrs, range 18-66)	Purposive sample of NHS physiotherapy referrals.	Semi-structured interviews, thematic analysis	1) Symptoms; 2) Diagnosis trajectory; 3) Factors prompting diagnosis and referral for physiotherapy; 4) The meaning of diagnosis; 5) Pre-trial symptom management; 6) Prior experiences of physiotherapy; 7) Attitude to the use of physiotherapy to treat JHS.

Authors	Location	Diagnosis	Sample size (n), sex and age	Sampling procedure	Data collection	Themes identified
(Schmidt *et al.*, 2015)	United Kingdom	JHS	11: all women (mean age 34 yrs, range 22-55)	Opportunity sample of women attending a pain management clinic.	Semi-structured interviews, IPA	1) Keeping pain at a manageable level; 2) Is it worth it? 3) Influence of pain intensity; 4) Unpredictability of pain; 5) Exerting control and 6) Emotional cost of pain.
(Simmonds and Keer, 2007)	United Kingdom	JHS or EDS-HT	946: 906 women, 40 men (mean age and age range unclear)	Opportunity sample of support group members (HMSA and EDS-UK)	Written narrative feedback, Thematic Analysis	1) Physiotherapist as a partner; 2) Communication, hand on guidance and feedback; 3) Knowledge, experience and safety.
(Terry *et al.*, 2015)	United Kingdom	JHS	25: 22 women, 3 men (mean age 38.2 yrs, range 19-66)	Purposive sample of support group members (HMSA) & local NHS physiotherapy patients.	Focus groups, Thematic Analysis	1) The impact of JHS; 2) JHS as a poorly understood condition; 3) Receiving a diagnosis; 4) JHS management and self-care.

Abbreviations: EDNF: Ehlers-Danlos National Foundation, EDS-HT: Ehlers-Danlos Syndrome (Hypermobility Type, HMSA: EDS-UK: Ehlers-Danlos Support UK, Hypermobility Syndromes Association, IPA: Interpretative phenomenological analysis, JHS: Joint Hypermobility Syndrome, PH: phenomenological hermeneutical analysis.

Table 4.3: Methodological rigour of included papers, appraised using the CASP checklist for qualitative papers.

Study first authors	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment design appropriate to address the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	Value of the research? Contribution to knowledge/ transferability	Overall quality score & rating*
(Berglund *et al.*, 2000)	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	9 High
(Berglund *et al.*, 2010)	Yes	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	8 High
(Bovet *et al.*, 2016)	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	8 High
(De Baets *et al.*, 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
(Palmer *et al.*, 2016b)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High

(Palmer *et al.*, 2016a)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
(Schmidt *et al.*, 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
(Simmonds *et al.*, 2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
(Terry *et al.*, 2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High

*Scored according to the CASP checklist of 10 items; '*yes*'= 1 point, '*can't tell'*= 0 points, '*no*'= -1 points. Maximum score=10 points. Quality rating defined as high methodological quality= score ≥8 points, medium quality= 4-7 points and poor quality = ≤3 points.

4.4 Synthesis Findings

Findings relating to adults' experiences of living with JHS and EDS were predominantly similar across papers and grouped into five major overarching themes: lack of professional understanding; social stigma; restricted life; trying to "keep up"; and gaining control (Figure 4B). For each theme, quotations have been provided from included papers. Illustrative quotes representative of each theme are also presented in Appendix A.

4.5 Lack of Professional Understanding

4.5.1 Long Journey to Diagnosis

A widespread lack of awareness of JHS and EDS amongst healthcare professionals was a feature of all papers, which led to great delay in gaining a diagnosis. Patients being referred to a wide range of specialists was common and, in the absence of disease, many were told their problems were "*growing pains*" (Palmer *et al.*, 2016a), "*all in your head*" (Berglund *et al.*, 2010) or "*there must be something wrong in your mind*" (Berglund *et al.*, 2000). Many were labelled: "*psychosomatic*" (Berglund *et al.*, 2000) "*self-inflicted Munchausen Syndrome*" (Berglund *et al.*, 2010) or "*malingerer*" (Berglund *et al.*, 2000). Some participants did not feel believed by healthcare professionals "*it's…Psychological and you… just need to be a bit braver*" (Palmer *et al.*, 2016b). Many spoke of relief at discovering their diagnosis (Palmer *et al.*, 2016a), "*that helped me hugely psychologically*" (Terry *et al.*, 2015) as it provided recognition of their symptoms, a "*missing piece of the puzzle*" which took away uncertainties, equipping participants to make informed decisions about their care (De Baets *et al.*, 2017). However, for others it could be a struggle to find healthcare professionals with knowledge of JHS/EDS-HT, and they could become "*frustrated*"; "*I didn't want to be the educator*" (Bovet *et al.*, 2016).

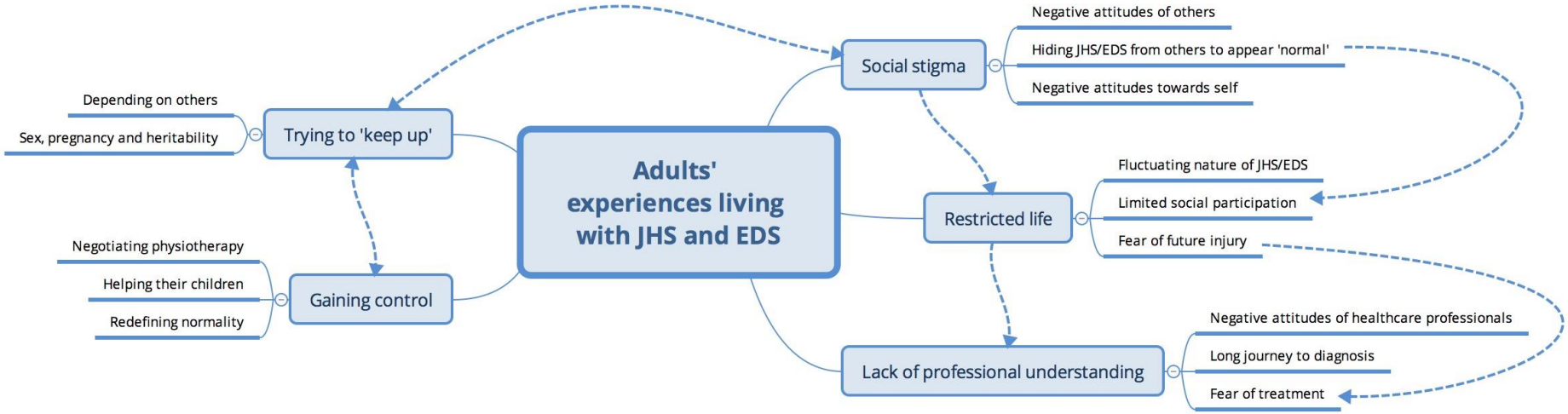


Figure 4B: Thematic schema illustrating the five main themes and fourteen subthemes. Arrows represent links between themes and subthemes. Abbreviations: EDS = Ehlers-Danlos Syndrome, JHS=Joint Hypermobility Syndrome

4.5.2 Negative Attitudes of Healthcare Professionals

Due to easy skin bruising, relatives were often accused of harming the patient with JHS or EDS (Berglund *et al.*, 2010, Berglund *et al.*, 2000). The novelty of their conditions meant participants were the subject of intense scrutiny by healthcare professionals and medical students. Participants described feeling "*humiliated*" when treated "*as objects*" during physical examinations, rather than being met with consideration and understanding (Berglund *et al.*, 2010). Patients described physiotherapy with inexperienced practitioners as "*useless*", "*diabolical… No help whatsoever*" (Simmonds *et al.*, 2017), many felt that their physiotherapists had "*given up*" (Palmer *et al.*, 2016a) and reported that exercises had worsened their pain or led to further injuries (Bovet *et al.*, 2016).

4.5.3 Fear of treatment

Many with JHS and EDS reported a poor reaction to local anaesthetics, thought to be due to the underlying collagen defect (Wiesmann *et al.*, 2014). This resulted in patients undergoing surgical or dental procedures being fully aware of severe pain: "*I remember the pain when they were cutting, oh, I still feel abused*" (Berglund *et al.*, 2000). Understandably, distressing experiences as well as specialists who may be "*dismissive*" of patients' symptoms (Bovet *et al.*, 2016) led to great fear of healthcare professionals, treatments and hospitals. Although, this could result in participants not getting the medical care they needed: "*I have stopped seeing doctors … I would rather suffer!*" (Berglund *et al.*, 2010).

4.6 Social Stigma

4.6.1 Negative attitudes of others

Participants were fearful of others' reactions when disclosing their JHS or EDS; only

describing it vaguely (De Baets *et al.*, 2017); "*If it gets around that I have EDS, it might mean a change in my situation at work*'' (Berglund *et al.*, 2000). Participants were reluctant to "*ruin*" others "*expectations and perceptions*" of them: "*You don't want people to start thinking 'Oh well, you know…We don't employ people with disabilities because this is what happens'*" (Terry *et al.*, 2015). Others were reluctant to appear to be complaining all the time (De Baets *et al.*, 2017). Participants spoke of being considered "*freaks*" (Berglund *et al.*, 2000) due to their hypermobility and stretchy skin. These negative attitudes were thought to be due to others' lack of knowledge and understanding (De Baets *et al.*, 2017). As children, participants were criticised by teachers for "*not performing as expected*" (Berglund *et al.*, 2000). As adults, the fluctuating nature of JHS/EDS symptoms contributed to a lack of support: "*If you're inconsistent as well, they sort of go 'she was alright with that last week'* (Terry *et al.*, 2015). Some speculated whether "*it would be better to have an amputated leg, so that people could see that I'm struggling.*" (De Baets *et al.*, 2017).

4.6.2 Hiding JHS and EDS from others in order to appear 'normal'

Participants sometimes chose not to tell friends or colleagues about their condition; hiding their scars and bruises in an effort to be treated like everyone else (Berglund *et al.*, 2000). Some feared the reactions of others (De Baets *et al.*, 2017). This was used as a means of gaining control, avoiding being seen as "*the odd one out*" (Terry *et al.*, 2015) by appearing normal and "*unrestricted*":

> "When I go out when I'm seen by other people, I'm trying to do things like the others so I try, I want people to see me like normal"
>
> (Schmidt et al., 2015)

However, the consequence of keeping up a front was wearing:

"[. .] *it's so exhausting mentally and physically to try and appear to be normal and do normal things throughout the day with everybody and pretend it's alright*" (Terry *et al.*, 2015)

4.6.3 Negative attitudes towards self

Those who had negative experiences with healthcare professionals felt insecure (Berglund *et al.*, 2000) and "*inferior*" (Berglund *et al.*, 2010). The differences in their physical appearance made participants feel "*embarrassed*" (Berglund *et al.*, 2000), "*ugly*" (Berglund *et al.*, 2000) and "*more ill than human*" (De Baets *et al.*, 2017). These negative feelings also linked to the theme 'trying to "keep up"' as participants felt self-directed anger when they had made their pain worse and had to give up activities, in addition to guilt, depression and frustration (Schmidt *et al.*, 2015).

4.7 Restricted Life

4.7.1 Fluctuating nature of JHS and EDS

The unpredictability of JHS and EDS symptoms made planning ahead difficult and had a great impact on participants' lives:

> "It's not always instantly that you're going to get the flare. It'll be that evening or the following day that you'll flare and so it's kind of like trial by error really" (Schmidt et al., 2015).

None had a regular structure for managing fatigue (De Baets *et al.*, 2017). Participants' activities could be very limited on the days that they were in pain, but on better days they could "*jump over small houses*" (Berglund *et al.*, 2000). However, this also carried a risk of overexertion: "*On days when I feel better…I use all my energy until I'm completely exhausted, then I am unable to do anything*" (De Baets *et al.*, 2017). Pain interfered with participants' moods: "*If the pain is reduced I feel my* [mood] *going back up…So I know it's all to do with the excruciating pain.*" (Schmidt *et al.*, 2015). Severe pain episodes had made others fearful: *"I'm always scared when I go back into big heavy pain…I always get scared that I'll get … back like that.*" (Schmidt *et al.*, 2015).

4.7.2 Limited social participation

Participating in social activities was difficult due to the limited range of activities

people with JHS or EDS can do without harming themselves (Berglund *et al.*, 2000). Peer pressure and the high expectations of teachers made school years "*tough*", particularly if participants did not perform as well as expected due to their symptoms (Berglund *et al.*, 2000). Chronic daily pain associated with EDS also limited participation in hobbies (De Baets *et al.*, 2017, Palmer *et al.*, 2016a), social activities (Berglund *et al.*, 2000, De Baets *et al.*, 2017) and restricting what participants could choose regarding education and job opportunities (Berglund *et al.*, 2000). Frustratingly, some participants were required to readjust their career plans (Berglund *et al.*, 2000). Others described retraining into different roles, making adaptations to their work, switching to part-time work, or stopping completely (Schmidt *et al.*, 2015).

4.7.3 Fear of future injury

Participants analysed the benefit of an activity versus the pain or potential injury that could follow: "*Something that is potentially high risk of dislocation then it's just not worth doing it*" (Schmidt *et al.*, 2015). Even short outings required a great deal of planning to avoid harm; "*walking the dogs I have to be careful where I walk them, what I do, whether the ground's level… I have to be really aware of my surroundings"* (Schmidt *et al.*, 2015).

"*Injury fears*" led many participants to be less sociable than they wanted to be, as symptoms or the threat of future injury made it difficult to plan ahead "*I cannot, for example,* [decide] *to see my friends, because I don't know how I'm going to be in three days. I might be in pain*" (Schmidt *et al.*, 2015) and this caused emotional distress: *"I'm in a constant state of anxiety, waiting for the next injury and trying to pre-empt anything that's going to cause it"* (Terry *et al.*, 2015). This also links to the theme 'fear of treatment' as participants were wary of becoming injured far from home: "*If I fall I fear I will get injured and have to go to a hospital that I am not familiar with!"* (Berglund *et al.*, 2000).

4.8 Trying to "Keep Up"

4.8.1 Depending on others

"Keeping up" with others who did not have JHS or EDS was physically and emotionally "*draining*" and "*difficult*" for participants (Berglund *et al.*, 2000). This theme also links to 'social stigma' as participants did not want to ruin others' perceptions of themselves by admitting that they had any problems fulfilling their expectations (Terry *et al.*, 2015, De Baets *et al.*, 2017). Participants had to restructure activities and depend on those around them for help to manage daily life (De Baets *et al.*, 2017, Berglund *et al.*, 2000), but this brought guilt, depression and frustration as participants could not complete the tasks expected of them without the support of their family: "*If I'm having a flare up I can't cook a meal … I have to get my eldest daughter to make a dinner, but then, it depresses me because I feel like I'm not doing my role as a mother*" (Schmidt *et al.*, 2015). Having an understanding partner and family was cited as a great source of support, helping to reduce feelings of guilt (De Baets *et al.*, 2017).

4.8.2 Sex, pregnancy and heritability

Pregnancy complications in all types of EDS can include pelvic pain and instability, profuse bleeding, complicated perineal injuries, premature rupture of membranes and preterm delivery (Lind and Wallenburg, 2002). One woman defended her decision to never become pregnant, as she did not want to: "*walk around terrified for nine months*" (Berglund *et al.*, 2000). Others feared their children inheriting their condition: *"I am not getting pregnant if I know my child will have EDS… Because I don't want him or her to go through the same struggle that I have been through.*" (Berglund *et al.*, 2000). However, others cited that, while a difficult choice, gaining a concrete diagnosis had helped them to make an informed decision about whether or not to have children; "*the information gained through the diagnosis ensured that one can make an informed choice"* (De Baets *et al.*, 2017). The support of a gynaecologist with experience of JHS/EDS was therefore valuable: "*If I had not had her I might not have had children. She gave me a lot of support, lots of explanation*

and she has a lot of experience" (De Baets *et al.*, 2017).

4.9 Gaining Control

4.9.1 Negotiating physiotherapy

Patients in the UK reported that they were usually offered up to six physiotherapy sessions for one painful joint. However, due to their susceptibility to injury participants with JHS and EDS experienced pain and weakness in multiple joints throughout their body: "*they often concentrate on one area and then forget that the rest of the body hurts as well"* (Palmer *et al.*, 2016b). Physiotherapists could struggle to know how to treat patients, as *"hypermobility is totally the opposite of what they're expecting and they can't understand that*" (Palmer *et al.*, 2016b). Participants described a cycle of decline as recommended exercises could make their pain "*feel* WORSE" (Simmonds *et al.*, 2017) "*and then the treatment's over because you only get a few sessions*" (Palmer *et al.*, 2016b). In contrast, "*Hands-on*" (Simmonds *et al.*, 2017) "*whole body*" (Bovet *et al.*, 2016) input and advice from a physiotherapist with a specialist interest in JHS and EDS was very helpful: *"…It's been amazing; I feel like it's been worthwhile…And I've been really enjoying it*" (Terry *et al.*, 2015); *"…It has made all the difference*" (Simmonds *et al.*, 2017). Some indicated that due to JHS/EDS-HT they were less likely to have effective proprioception, so finding a physiotherapist that could accommodate these differences was seen as greatly beneficial:

> "I found heavily guided exercise the most beneficial; I think that I am less likely to have awareness of how well I am completing the set tasks than "normal" people. My last physio saw me for far longer than usual … so that she could keep checking my effectiveness of repetition afterwards, this enabled me to have plenty of feedback to keep my energy from being wasted by mis-performing exercises"
>
> (Simmonds *et al.*, 2017)

Participants cited a holistic understanding of "*both me as a person and my physical condition*" as making the relationship between patient and physiotherapist work

(Simmonds *et al.*, 2017). Recognising the limits of physiotherapy was also important "[The physiotherapist] *said, 'You know, I can only give you so many exercises. I can't change your physiology*'" (Palmer *et al.*, 2016a).

4.9.2 Helping their children

Knowing their own struggles and difficulties it was not easy for parents with EDS and JHS to advise their affected children regarding educational decisions, career paths or participation in sporting activities (Berglund *et al.*, 2000, De Baets *et al.*, 2017). Parents were also conflicted in whether to protect their children from injury or encourage them to take on activities without fearing their condition (De Baets *et al.*, 2017, Berglund *et al.*, 2000). Mothers expressed a need to act as a positive role model for their children (Palmer *et al.*, 2016a, De Baets *et al.*, 2017); actively engaging with their children gave participants an incentive to be active, and took their mind off their illness (De Baets *et al.*, 2017). Being able to satisfy the needs of their family and children contributed positively to their identity as a '*good mother*' and boosted self-esteem (De Baets *et al.*, 2017).

4.9.3 Redefining normality

While participants accepted the lifelong nature of their condition as "*you're going to have it forever*" (Palmer *et al.*, 2016b); "*there is no cure for it*" (De Baets *et al.*, 2017), many found ways to pace their activities to "*live with pain that comes and goes*" (Berglund *et al.*, 2000): "*I have this balancing act, if I do too much it all hurts, don't do enough, it all hurts, do it just right, I'm okay*" (Terry *et al.*, 2015).

Others broke activities down into smaller steps, or discovered novel ways of completing a goal: "*I won't be able to do something throughout, I have to sort of break it up into pieces and do it bit by bit by bit*" (Schmidt *et al.*, 2015), "*you're probably going to be like this always, you need to think of different ways to manage different things"* (Palmer *et al.*, 2016b). Participants adopted a positive mental outlook in respect to their limitations: "[physiotherapists] *reassured me that it's not the end of the world and you know sometimes you have a bad week but it doesn't mean that you won't then have a good week*" (Palmer *et al.*, 2016b). This changed

their perceptions of what successfully managing their own condition meant to them: "*I think measuring success should be more about reaching a point of continuity where you know you might not be great all the time or you might not be really bad all the time but you're manageable*" (Palmer *et al.*, 2016b).

4.10 Discussion

4.10.1 Summary of Evidence

JHS and EDS have a substantial impact on participants' activities of daily living. The unpredictable nature of repeated injuries and associated pain made some cautious and fearful, limiting social and physical activities. Others experienced a lack of understanding and empathy from healthcare professionals and from their friends and family, largely due to the invisible nature of the condition. Participants mentioned the need for increased awareness of associated issues with local anesthetics (Berglund *et al.*, 2000, Berglund *et al.*, 2010). Studies have indicated a lack of training in JHS/EDS for healthcare professionals (Ross and Grahame, 2011). Although a recently published Royal College of General Practitioners (RCGP) EDS toolkit has made great efforts to improve awareness amongst UK GPs, (Reinhold *et al.*, 2018) there is still much work to be done to improve recognition of JHS and EDS.

Many hid their condition from others in order to appear 'normal', but this was exhausting to maintain, and participants felt intense guilt and depression. Stigma in JHS/EDS-HT may have negative consequences for self-care and psychological wellbeing including decreased self-efficacy and catastrophising attitudes to pain (Waugh *et al.*, 2014). A common stigma management strategy involves patients disclosing their condition, with the aim to educate others and improve understanding (Lennon *et al.*, 1989, Poindexter and Shippy, 2010, Brown *et al.*, 2018). Although no intervention for JHS/EDS related stigma currently exists, training in communication skills at an individual level may have positive educational effects; improving people's ability to communicate the impact of JHS/EDS to the general public. By improving others' knowledge of their condition, this may help to

reduce misunderstanding and improve awareness, which can increase the patient's own self-confidence and self-esteem (Heijnders and Van Der Meij, 2006).

The inability to keep up with their well peers and intrusion of symptoms made it difficult for those with JHS and EDS to function socially. Nonetheless, some participants adopted positive attitudes to their limitations, maintaining exercise regimes and pacing their activities. Activity pacing, graded exercise therapy, reducing working hours, and access to equipment and adaptations have been suggested as prospective management options in EDS-HT, in order to maintain independence (Hakim *et al.*, 2017). Evidence from RA literature indicates that employing coping strategies such as planning, adjusting daily activities and using assistive devices to be important strategies for adapting to pain (Bergstrom *et al.*, 2017). Future research in this area may wish to address interventions to promote independence, in order to better support those with JHS/EDS-HT.

Women with JHS and EDS were fearful of passing on their genes to their children. Some preferred to avoid the risk of pregnancy-related injuries and complications entirely. Studies examining potential risks associated with pregnancy have shown mixed results. While recent papers have shown positive results for women with JHS/EDS-HT, with few pregnancy complications (Castori *et al.*, 2012b), some studies have indicated risks of rapid labour, rapid delivery (Castori *et al.*, 2010), increases in joint laxity and pain (Volkov *et al.*, 2007). Therefore, personalised approaches to JHS/EDS-HT maternity care and planning have been recommended to ensure best practice in maternity care (Camerota *et al.*, 2011).

Where participants with JHS/EDS had affected children, many parents acted as role models, seeking to better control their child's treatments and encourage self-management. For patients, discovering a pattern of heritable genetic disease in their family can create fear of the future (Finkler *et al.*, 2003). However, awareness of potential genetic relationships can also give an individual a sense of mastery and control over their condition and its associated treatment (Finkler *et al.*, 2003).

4.10.2 Strengths and limitations

To ensure validity of findings, a second reviewer independently reviewed all of the included papers for methodological quality. The review included EDS and JHS related qualitative research from a range of countries with adult participants of both genders. Although a relatively small number of papers were included for analysis, email contact with JHS and EDS researchers confirmed that this review has examined all available qualitative evidence from 1990 to date. The methodological quality of the included papers was high (all CASP scores ≥8).

Participants' average ages in the included studies varied from 33 years (Palmer *et al.*, 2016a) to 43.5 years (Berglund *et al.*, 2010), see Table 4.2). The studies reported age somewhat differently. In one study only the range, not the mean age was indicated (Berglund *et al.*, 2000), in another, age was indicated by decades (Berglund *et al.*, 2010), and in another, participants' ages were not disclosed (Simmonds *et al.*, 2017). Not stating participants age range, mean age or standard deviation can make it difficult to compare results between studies. As joint laxity is known to decrease with age (Beighton *et al.*, 1973, Bridges *et al.*, 1992, Larsson *et al.*, 1993, Remvig *et al.*, 2007), and standardisation of expected joint laxity at different ages has yet to be researched, it is important for authors to include as broad a range of participant ages as possible to reflect the variations in joint laxity over the lifespan.

The recruitment of participants across all EDS subtypes (Berglund *et al.*, 2000, Berglund *et al.*, 2010) is a potential limitation. It is difficult to ascertain from the results whether included participants had the hypermobile, vascular, classical or another subtype of EDS, as this PhD thesis focuses on EDS-HT.

A further limitation is the self-report nature of the JHS/EDS diagnosis in the majority of included papers. Although some participants were recruited using medical records (Palmer *et al.*, 2016a, Palmer *et al.*, 2016b, De Baets *et al.*, 2017, Terry *et al.*, 2015) the majority were recruited from support groups. Self-reported diagnosis can be more prone to bias than clinically assessed JHS/EDS-HT, due to the potential for false-positive self-reporting of the condition, or confusion regarding changes in nosology over time. In order to mitigate these risks in populations that

cannot be clinically assessed, some researchers have used clinical assessment measures of hypermobility such as the Hakim and Grahame five-part questionnaire (5PQ; (Hakim and Grahame, 2003). While not completely free from bias, when a cutoff score of a score ≥2 is applied it has high sensitivity (80-85%) and specificity (80-90%) to the cutoff score for hypermobility as assessed physically: a Beighton score of 4 out of 9 (Hakim and Grahame, 2003). Despite studies suggesting that the 5PQ has been shown to have conflicting evidence in terms of reliability (Juul-Kristensen *et al.*, 2017) for future measures of self-reported diagnosis, this may be a more robust option in the remote clinical assessment of hypermobility than self-reported diagnosis alone.

4.10.3 Implications for research

The emotional and physical impact of JHS and EDS on adults is substantial. This is the first qualitative systematic literature review of its kind examining JHS and EDS. By focusing on, and consolidating findings from qualitative studies of participants' lived experiences, this review has identified a range of common findings across the included papers. This thematic synthesis has highlighted potential avenues for research and clinical outcomes that are likely to be considered important by people with JHS/EDS. While JHS/EDS has been associated with significant rates of anxiety, depression and panic disorders compared to the general population, systematic reviews have focused on quantitative data (Smith *et al.*, 2014b). Relatively little attention has been paid to the first-hand accounts of participants and how they cope with JHS/EDS, and this review brings a new focus and insight into these experiences.

Our findings provide first-hand support for the need for individualised care for this patient population, in keeping with recommendations for inclusive, multidisciplinary treatment and support (Engelbert *et al.*, 2017, Castori *et al.*, 2012a, Palmer *et al.*, 2016b, De Baets *et al.*, 2017). Potential ideas for interventions to better support people with JHS/EDS, and those involved in their care, have been suggested by the findings.

Although hypermobility is known to affect Black and Asian populations to a greater extent (Connelly, 2015), very few ethnically diverse participants have been

involved in JHS and EDS research compared to participants of white ethnicity. Furthermore, although proportionately fewer are affected, the views of men within JHS/EDS research have yet to be explored in great depth. Therefore, future research with these under-researched populations would be very valuable.

4.11 Conclusion

The aim of this chapter was to understand the lived experiences of people with JHS and EDS, by conducting a systematic review of the literature. Thematic synthesis of these results provide new insight into the lived experience of adults with JHS and EDS, including participants' anxieties, limitations to their social lives and physical activities, a lack of recognition of the condition, and the need for multidisciplinary care.

Though a comprehensive overview of all qualitative data relating to JHS and EDS to date, the results of this review may not have covered all factors relevant to the lived experience and impact of JHS and EDS on individuals. The candidate was interested to hear more from participants with JHS/EDS-HT about the complex experience of managing a chronic condition and its impact on their lives, including their work lives, education and social activities. Although participants identified physiotherapy, pacing activity and looking for alternative ways to achieve their goals as a means to better self-manage their JHS and EDS, other means of self-management, such as patient education; environmental modifications and social support received little mention in this synthesis of the literature. Likewise, there was little evidence regarding the information resources available for self-management, or how participants utilised knowledge to self-manage their JHS or EDS. Therefore, in order to gain a greater understating of how participants cope with their condition, a further objective is to understand how participants cope with their JHS/EDS-HT.

To expand on this, the aim of the next chapter is to explore the psychosocial, cognitive and behavioural impact, with a focus on JHS/EDS-HT. The decision was made to focus on JHS/EDS-HT due to the subtype being the most common of all the EDS subtypes. While the originally intention of this chapter was to focus on papers that had recruited adults with JHS and EDS-HT only, two key papers recruited participants across all subtypes of EDS (Berglund *et al.*, 2010, Berglund *et al.*, 2000).

For this reason, the inclusion criteria for this review was broadened to better reflect the qualitative literature available at the time of the review, and this thesis will now resume focus on the EDS-HT subtype.

5 Chapter 5, Study 2: Exploring the psychosocial impact of Joint Hypermobility and Ehlers-Danlos Syndrome in adult men and women.

5.1 Background

The qualitative study reported in this chapter explored the lived experiences and impact of Joint Hypermobility and Ehlers-Danlos syndrome Hypermobility Type on men and women from across the UK. An edited version of this chapter was published in the journal Disability and Rehabilitation in July 2019:

> Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2019) "Understanding the psychosocial impact of joint hypermobility syndrome and Ehlers–Danlos syndrome hypermobility type: a qualitative interview study", *Disability and Rehabilitation*, pp. 1-10. doi: 10.1080/09638288.2019.1641848.

The exploratory systematic review detailed in Study 1 examined and gave a comprehensive overview of what has previously been published regarding adults' lived experiences of joint hypermobility syndrome (JHS) and Ehlers-Danlos syndrome (EDS). Having explored the lived experiences of JHS and EDS within the published literature, it was deemed important to further explore and expand upon areas that had not been covered in earlier studies, such as approaches towards self-management and coping.

5.1.1 Overall study aim:

To explore the psychosocial**,** cognitive and behavioural impact of JHS and EDS-HT. The results will allow the design and development of future interventions and services to support those with JHS/EDS-HT.

5.1.2 Objectives:

1. To identify the psychosocial impact of JHS/EDS-HT by examining participants' lived experiences**.**

2. To identify characteristics of effective coping with JHS/EDS-HT.

5.2 Ethical approval

Approval for the study was obtained from the University of the West of England Faculty Research Degrees Committee (HAS.16.06.161, Appendix B), and the West London and GTAC Research Ethics Committee (16/LO/L511, Appendix C).

5.3 Participant recruitment

The proposed plan was to recruit participants with a clinically confirmed diagnosis of JHS or EDS-HT, through established research links with two local NHS Trusts in the South West of England. Individuals with a self-reported diagnosis of JHS, EDS-HT or both were also planned to be recruited through established research links with two patient support groups, The Hypermobility Syndromes Association (HMSA) and Ehlers-Danlos Support UK (EDS-UK). The proposed target size was 15-20 participants and due to the qualitative nature of the research a sample size calculation was not specified.

However, within 11 days of EDS-UK placing the advertisement, 311 potential participants expressed an interest in taking part. Due to the large recruitment response, the decision was made to recruit from one NHS Trust and the EDS-UK social media advertisements only. As a result of the wide response, many participants expressing interest in the study were also members of the HMSA (n=25 of n=140 potential participants who met the inclusion critiera, 17.85% of the sample).

It is acknowledged that while attempts were made to recruit participants from local NHS cohorts, the majority of participants were members of support groups. Although a limitation in terms of selection bias, these recruitment methods were the most effective for recruiting a clinically representative and geographically diverse sample of participants, thereby improving the generalisability of the sample to other JHS/EDS-HT populations.

Research and Development approval was obtained for the NHS Trust site from which potential participants were contacted. The principal Investigator physiotherapist at the NHS trust identified participants who had received physiotherapy treatment for JHS or EDS-HT within the last two years (2015-2016). Those who met the inclusion criteria were posted a participant recruitment letter and information sheets, demographic and screening questionnaires, and a reply slip (Appendix D-H) by the lead researcher. It was made clear to potential participants that should they decline to take part, their care would not be affected in any way. The contact details of the lead investigator were provided and participants were encouraged to ask any questions. To express interest in the study, participants returned their signed informed consent form, demographic questionnaires (Appendix G), Hospital Anxiety and Depression (HADS) questionnaire and reply slip (Appendix H and D), to the researcher in the stamped-addressed envelopes provided. Alternatively, if they had access to the internet, potential participants had the option to follow a secure link and, using a password provided within the invitation letter, could submit an online version of their responses using Qualtrics software (2017, Qualtrics.com, Washington USA). Qualtrics is an online-based automated survey development system that records participant responses to allow for automated, password-protected data collection from any participant with an internet connection and the survey password. The Qualtrics online survey featured the same informed consent form (Appendix F), demographic questionnaires (Appendix G), and Hospital Anxiety and Depression Scale (HADS) questionnaire (Zigmond and Snaith, 1983), Appendix H) as the post versions sent to prospective NHS participants.

The present study was also advertised online. Participant information sheets and details about the study were advertised publicly in the form of advertisements (Appendix I) in addition to the Participant Information Sheet (Appendix E) and a secure link and password to the online Qualtrics survey. The advertisement featured details about the study, inclusion and exclusion criteria and the email address of the principal investigator. Participants indicated interest by either emailing the principal investigator, or following the link provided, which gave participants the Participant Information Sheet, consent form, and provided the lead investigator with their details.

5.3.1 Inclusion Criteria

Participants were required to be adults over the age of 18 years, with a self-reported diagnosis of either JHS or EDS-HT, who were able to understand and communicate in English (with interpreter if required), and who were able and willing to give informed consent. Participants with a diagnosis of fibromyalgia, in addition to a diagnosis of JHS or EDS-HT were included, as those with JHS are significantly more likely to self-report a diagnosis of fibromyalgia, compared to other rheumatology patients (30% vs. 8%, (Hudson *et al.*, 1995); 27.3% vs. 11.4%, (Acasuso-Diaz and Collantes-Estevez, 1998). To screen for any erroneous self-diagnosis, participants were screened using the Hakim & Grahame (2003) 5-item questionnaire, which has an 80-90% specificity and 80-85% sensitivity in identifying GJH.

5.3.2 Exclusion criteria

Patients in whom pain was caused by another musculoskeletal disorder such as osteoarthritis, inflammatory or autoimmune arthritis, or those suffering from other forms of EDS were excluded from the study. Those with high levels of anxiety or depression as measured by the HADS (scores ≥15 on either subscale) were excluded from the study, at the request of the West London and GTAC Research Ethics Committee, as it was felt that a telephone interview may be too distressing for a participant with clinically significant anxiety or depression.

5.4 Participant Sampling

Of the 311 initial responses, 22 were incomplete, giving 289 potential participants (281 women and 8 men). At this stage, an error was detected in the online version of the Hospital Anxiety and Depression Scale (HADS); the last two items on the subscale had not been published with the other items on the Qualtrics survey platform. These were item 13; "*I get sudden feelings of panic*" and item 14 "*I can enjoy a good book or radio or TV program*". Participants who had expressed interest were contacted to explain the mistake and were asked to repeat the HADS questionnaire.
141 participants from the original cohort repeated the HADS. Seven new participants (all women) also completed the corrected online HADS questionnaires. Of these 148, three responses were incomplete, and five did not meet the inclusion criteria giving a total potential participant cohort of 140. Reasons for exclusion included a participant aged under 18 (n=1); and a diagnosis of: Marfan Syndrome (n=1), Osteoarthritis (n=1), Complex Regional Pain Syndrome (n=1), and Lupus (n=1). After applying HADS screening criteria, (HADS-A ≤15, HADS-D ≤15), 114 participants (109 women, 4 men) with an average age of 36 years (range 18-70) were considered for inclusion. The participant sampling process is outlined in Figure 5A below.

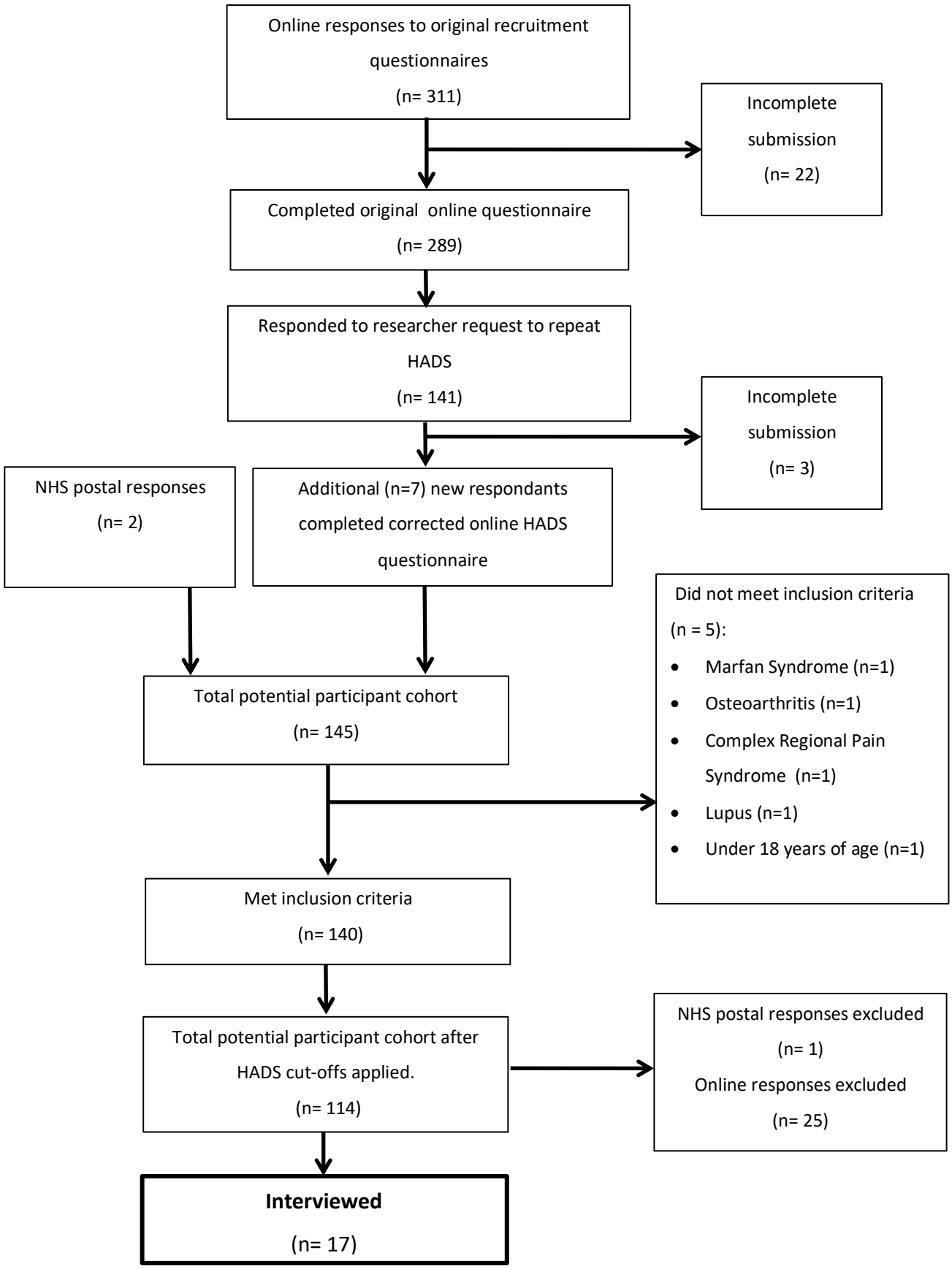
Although a small number of international members of EDS-UK and the HMSA expressed an interest in taking part, all included participants were from the UK, met the inclusion criteria and were eligible to participate. This was checked using estimated location information collected by Qualtrics, in addition to the inclusion criteria, before each included participant (n=17) was contacted by email to arrange an interview. This decision was made after extensive reflection and discussion with the supervisory team, due to the potential for differences in the treatment provided for JHS/EDS-HT in the UK compared to other countries, as well as differences in terms of cost and ease of access to healthcare. For example, a comparison of treatment for RA between the US and UK noted a number of significant treatment differences; participants in the US had significantly higher socioeconomic status, were more able to afford private health insurance, and so had improved access to

RA care and expensive drugs such as biologics (Chung *et al.*, 2010). In comparison, participants in the UK were more likely to be taking comparatively cheaper non-steroidal anti-inflammatory drugs, which may be due to the differences between private and universal healthcare systems (Chung *et al.*, 2010).

In terms of recruitment from the participating NHS trust, 21 patients met the inclusion criteria and were eligible to be contacted via post. Completed reply slips were received from 2 prospective participants. Of the two prospective NHS participants, one was ineligible due to a high HADS-D score (>15) and was excluded with telephone follow-up to thank them for their interest. In total, one participant from the participating NHS trust took part in the telephone interviews.

Although efforts were made to purposively sample participants in order to ensure diversity, these participants may not be representative of all UK patients with JHS/EDS-HT, and there are some key factors to consider between participants from the NHS trust and patient support groups. For example, members of patient support groups may have had more access to written information about their condition, compared to patients recruited from an NHS trust. Likewise, it is possible that members of a patient support group might have better access to social support and understanding from other members about their condition, compared to those without these links, who may be more isolated (Clark and Knight, 2017). While having only a single NHS-recruited participant made it difficult to compare and contrast these differences, care was taken to consider whether differences in access to support groups and social support may have had an impact on participants' lived experiences.

Figure 5A: Participant sampling process



5.4.1 The Sampling Frame

Participants were purposively sampled based on criteria relevant to JHS and EDS-HT research as depicted by the participant sampling frame in Figure 5B, including age, gender, ethnicity, degree of hypermobility and levels of anxiety and depression. Participants were sampled from across the UK. For each category of participants according to the sampling frame (such as women under the age of 35), a numbered list was generated listing all participants who met those criteria using Statistical Package for the Social Sciences (SPSS; version 25). Participants in the list were then randomly selected using an online, custom-range true random number generator (www.random.org, Randomness and Integrity Services Ltd, Dublin, Ireland). The reasoning and background literature supporting these sampling choices are outlined below.

5.4.1.1 Generalised Joint Hypermobility (GJH)

Participants were categorised by their Hakim & Grahame (2003) Five-Point questionnaire score (for questions, see Table 2.4, Chapter 2). The self-report questionnaire was used to screen for clinically significant GJH as it has high sensitivity (80-85%) and specificity (80-90%) when compared to a score of ≥4 on the Beighton score (Hakim & Grahame, 2003). An affirmative answer to two or more questionnaires indicates GJH, and in the sampling frame participants were classified by low (score 2-3), and high hypermobility (score 4-5).

5.4.1.2 Age

Generalised joint hypermobility (GJH; that is, hypermobility in a number of joints, without the associated pain of JHS/EDS-HT) tends to be more predominant in children compared to adults, with rates of GJH varying between 6.7% of schoolchildren from Kent (Carter and Wilkinson, 1964) and 51.1% in preschool

children from Parana, Brazil (Neves *et al.*, 2013). Studies have shown that the GJH shown in childhood tends to naturally decrease firstly as children hit puberty. In adults with GJH, the laxity also gradually reduces over time as people age (Jaffe *et al.*, 1988), (Larsson *et al.*, 1993) thought to be due to age- related degenerative changes in collagen levels in the articular cartilage over time (Verzijl *et al.*, 2000). The average age of participants in the present study was 36 years (range 18-70). While literature regarding the prevalence of JHS/EDS-HT over the lifetime is still minimal, it was recognised as important to hear from both participants at the younger age of the hypermobility range (<35 years) and from those older than 35. Therefore, for the purposes of sampling, participants were divided into two age groups, those under 35 years, and those older than 35.

5.4.1.3 Gender

Secondly, efforts were made to consider participants by gender, as JHS is significantly more prevalent in women compared to men (Hakim *et al.*, 2004, Remvig *et al.*, 2007, Seow *et al.*, 1999, Simmonds and Keer, 2007). While the true underlying reasons for such a difference may not have been identified, it is clear that JHS is significantly dominant in women, and this was reflected in our potential participant cohort. Therefore, in order to give equivalent attention to the experiences of men, participants were sorted in the sampling frame by self-identified gender.

5.4.1.4 Ethnicity

Some prior research has indicated that prevalence of GJH in participants may be higher in some ethnic groups than others, but these incidence rates are highly variable. For example, a survey of New Zealanders found GJH prevalence of 0% for those of European descent and 8.7% for Maori (Klemp *et al.*, 2002). Adult women and men from Karachi, Pakistan showed a BJHS prevalence of around 10% (Kumar *et al.*, 2006). An assessment of adults from Nigeria found 12.91% to have features of JHS (Didia *et al.*, 2002), while a GJH prevalence of 17% has been found for adults age

15-39 in Singapore population, who were of Chinese, Malay and Indian ethnicity (Seow *et al.*, 1999). Russek and Errico (2016) found A GJH prevalence of 26.2% and a JHS prevalence of 19.5% of healthy New York College students (Beighton Score ≥5/9, (Russek and Errico, 2016)), while 30% of all referrals to a Musculoskeletal Triage Clinic in London met the diagnostic criteria for JHS (Connelly, 2015). The highest prevalence has been reported in Omani women, where 55% of a physiotherapy patient group and 21% of a control group had JHS (Beighton score ≥4/9,(Clark and Simmonds, 2011). Although highly variable, prior research indicates that ethnicity is likely to have an impact on JHS prevalence. Therefore, to increase the diversity of the sample, potential participants of mixed ethnicity (7.01%) were sampled primarily, while those of white ethnicity (97.1%) were sampled as a secondary criterion.

5.4.1.5 Anxiety and depression

The 140 participants were screened for anxiety and depression, depending on their score on the HADS. Zigmond and Snaith (1983) originally recommended scoring between 0 and 7 on either HADS subscale as normal, a score of between 8 and 10 as mild anxiety or depression. In the present study, participants were sorted into 'Low' or 'High' anxiety or depression. For the low category, participants scored less than or equal to 10 on the anxiety (HADS-A) or depression (HADS-D) subscale, which would give a score of normal (score 0-7) or mild (score 8-10) anxiety or depression. For the high category, participants could score 11 to 15 on the anxiety (HADS-A) or depression (HADS-D) subscale. In accordance with similar studies of chronic conditions the cut-off score for each subscale was set at ≥15, described by Clover and colleagues as the '*gold standard*' for identifying clinically significant emotional distress (Clover *et al.*, 2009). This allowed participants with clinically significant anxiety or depression to take part, but prevented participants with severe expressions of either condition from being included (scores >15, (Zigmond and Snaith, 1983, Snaith, 2003). At the request of the West London and GTAC Research Ethics Committee, those with severe anxiety or depression were excluded from the

study, as it was felt that a telephone interview may be too distressing for a participant with clinically significant anxiety or depression.

Figure 5B: Participant Sampling Frame (n=114).

Primary criteria										
		Hakim & Grahame (2003) Five-Point Questionnaire		Ethnicity	HADS-A score		HADS-D score			
		>2-3	>4	Mixed:	Low ≤10	High 11-15	Low ≤10	High 11-15		
Age range	Adults (18-35 years)	1-2[a] (n=6[b])	1-2[a] (n=42[b])	1-2[a] (n=4[b])	1-2[a] (n=32[b])	1-2[a] (n=22[b])	1-2[a] (n=41[b])	1-2[a] (n=13[b])	Female	Gender
			1-2 (n=1[b])		1-2[a] (n=1[b])		1-2[a] (n=1[b])		Male	
	Adults (>35 years)	1-2[a] (n=5[b])	1-2[a] (n=50[b])	1-2[a] (n=3[b])	1-2[a] (n=29[b])	1-2[a] (n=26[b])	1-2[a] (n=31[b])	1-2[a] (n=24[b])	Female	
			1-2[a] (n=3[b])	1-2[a] (n=1[b])	1-2[a] (n=1[b])	1-2[a] (n=2[b])	1-2[a] (n=2[b])	1-2[a] (n=1[b])	Male	
Secondary Criteria										
Diagnosis of Fibromyalgia (29.4% of sample)										
White ethnicity (97.1% of sample)										

a= Planned number of each participants in each criteria, b= number of participants in each criteria. However, it should be noted that one participant may fit into multiple criteria, therefore these numbers are for guidance only. Abbreviations: HADS-A= Hospital Anxiety and Depression Scale- Anxiety subscale, HADS-D= Hospital Anxiety and Depression Scale- Depression subscale.

5.5 Participants

A total of 17 people (14 women, 3 men) took part in the study. Participants ranged in age from 22 to 70 years (mean= 38.41 years). Pseudonyms have been used throughout to ensure confidentiality. All had a diagnosis of Ehlers-Danlos Type Three (EDS-III), Ehlers-Danlos Syndrome Hypermobility type (EDS-HT) or Joint Hypermobility Syndrome (JHS), depending on when they were diagnosed, which was due to the variations in nomenclature and categorisation of Ehlers-Danlos Syndrome over time.

A sample size of between 15 and 20 participants had been estimated for the study, the decision was made to cease recruitment at 17 interviews as no new themes were apparent from the interview data collected. The study was therefore deemed to have reached saturation point (Guest *et al.*, 2006).

Owing to the nature of the study, these were self-confirmed diagnoses, but all met the Hakim and Grahame (2003) Five-Point Score cut-off for identifying generalised joint hypermobility (GJH; a score ≥2). Many had dual diagnosis, that is, having being diagnosed with both JHS and EDS-HT over time. Five participants (4 women, 1 man, 29.4% of the final sample) also had a diagnosis of Fibromyalgia, which is closely comparable to rates of Fibromyalgia in other populations who have JHS (27.3% (Acasuso-Diaz and Collantes-Estevez, 1998); 30% (Hudson *et al.*, 1995). Participant demographics are presented in Table 5.1.

Table 5.1: Participant demographics of the Study 2 qualitative sample (n=17)

ID	Name	Age	Gender	Ethnicity	Self-described occupation	Diagnosis	5PQ score*	Anxiety (HADS-A)	Depression (HADS-D)	Fibromyalgia diagnosis
001	Rhiannon	28	Female	White	Postgraduate student	JHS	3	5	10	No
002	Jake	39	Male	Mixed: White & Asian	Postgraduate student	EDS-III	3	5	6	No
003	Roger	36	Male	White	Self-employed	EDS-HT	5	13	10	No
004	Dana	28	Female	White	Not in paid employment	JHS	2	12	6	Yes
005	Nigel	39	Male	White	Office work	JHS/EDS-HT	4	13	13	Yes
006	Lauren	52	Female	White	Retired	EDS-III	4	10	13	Yes
007	Emily	22	Female	Mixed: White & Indian	Postgraduate student	JHS/EDS-HT	5	4	5	No
008	Georgina	43	Female	White	Office work (reduced hours)	JHS	2	10	11	Yes
009	Frances	24	Female	Mixed: White & Asian	Postgraduate student	JHS/EDS-HT	3	8	7	No
010	Rachel	63	Female	White	Retired	EDS-HT	5	9	7	No
011	Bryn	25	Female	White	Postgraduate student	JHS/EDS-HT	5	14	12	No
012	Tabitha	70	Female	White	Retired	JHS	3	13	8	No
013	Claire	40	Female	Mixed: White & Asian	Not in paid employment	EDS-HT	4	8	13	No
014	Anna	41	Female	White	Office work (reduced hours)	JHS	5	14	12	Yes
015	Wendy	27	Female	White	Office work (reduced hours)	EDS-HT	2	8	9	No

ID	Name	Age	Gender	Ethnicity	Self-described occupation	Diagnosis	5PQ score*	Anxiety (HADS-A)	Depression (HADS-D)	Fibromyalgia diagnosis
016	Mandy	31	Female	White	Teacher (reduced hours)	JHS/EDS-HT	5	3	8	No
017	Jackie	45	Female	Mixed: White & Asian	Office work (reduced hours)	JHS/EDS-HT	2	14	12	No

*5PQ Five Part Questionnaire Hypermobility Score, where scores ≥2 indicate hypermobility (Hakim & Grahame, 2003). Abbreviations: 5PQ = Five part questionnaire, a measure of hypermobility, EDS-HT= Ehlers-Danlos Syndrome Hypermobility Type, EDS-III= Ehlers-Danlos Type III, an earlier diagnostic term for EDS-HT, HADS-A= Hospital Anxiety and Depression Scale- Anxiety subscale, HADS-D= Hospital Anxiety and Depression Scale- Depression subscale, JHS= Joint Hypermobility Syndrome.

5.6 The interview protocol

The interviews followed the interview protocol outlined in Appendix J. These questions were developed using issues highlighted in the JHS and EDS-HT literature as a guide, in addition to the results of the systematic review and thematic synthesis examining all qualitative JHS and EDS research to date (Study 1). Due to the exploratory nature of the study, the questions were broad to allow participants to share their experiences. The protocol covered each participant's diagnosis classification (JHS, EDS-HT, or both) and diagnostic journey (e.g. thoughts and experiences of diagnosis and healthcare experiences). A larger section examined participants' symptoms (e.g. physical symptoms such as subluxations and dislocations or fatigue) and looked at the psychosocial impact of JHS/EDS-HT factors such as participants' daily activities (e.g. activities of daily living, whether any activities made symptoms worse), education and/or work life, relationships with others (e.g. friends, family, partner), social and leisure activities (sports, hobbies etc.) and the emotional impact. Later questions asked participants to identify what they had tried that had a beneficial impact on coping with their condition, whether physical (e.g. exercise such as Pilates or running, physiotherapy, stretching) or cognitive/emotional (e.g. relaxation, cognitive behavioural therapy (CBT), pain management). Participants were also asked about the invisible nature of JHS/EDS-HT compared to other conditions, their experiences of healthcare professionals and their recommendations to others with the same condition. Questions were ordered to make participation less onerous, with those relating to diagnosis at the beginning of the interview, and potentially sensitive questions nearer the end, in an attempt to mitigate any potential distress. In all correspondence the interview was framed as a 'friendly chat', due to the stressful and potentially negative connotations of the word 'interview'. Prior to conducting the interviews, the interview schedule was reviewed by the Patient Research Partner, subjected to a test interview with another PhD researcher, and regularly appraised after each participant interview, with questions reworded if necessary to ensure ease of understanding.

5.7 The distress protocol

A Distress Protocol (Appendix K) was designed and implemented to ensure that a valid, staged procedure and support was in place to safeguard any participant who became unduly distressed at the time of the interview. Although undoubtedly some memories were emotive to recall, no participants became tearful or suffered undue distress and all seemed content to share their experiences. As a result, the protocol was not needed during the interviews, however it was reassuring to have the protocol in place.

On completion of each interview participants were thanked for participating and asked whether there were any questions or topics that they would like to discuss that had not been covered already. Occasionally participants couldn't remember a word or the name of something they wanted to disclose. Participants were encouraged to send an email if they wished to add anything; Tabitha emailed with a word she remembered after the interview, which was later added to her transcript.

5.8 Data collection: Conducting interviews

Telephone interviews were conducted between August 2016 and March 2017. The interviews took place in a private office at the University of the West of England, Bristol at a time convenient to both parties, arranged in advance to ensure privacy and access to relevant notes (Smith, 2005). Recording was achieved through use of a Dictaphone and in-line recording adapter connected to the phone handset, with participants reminded that the call was being recorded at the start of each session. Interviews lasted from between 43 and 99 minutes (with a mean time of 74 minutes). To put each participant at ease, the format and aims of the interview were explained, anonymity assured, and each participant was given the opportunity to ask any questions before the interview questions commenced (Smith, 2005, Burnard, 1994).

Most participants were at home at the time of the interview; one participant took the call in their private office at work and another from their car. Occasionally participants were interrupted by external distractions such as the doorbell or family pets, and the interview paused if required. The majority of participants were alone when taking part in the interview.

One call had technical difficulties. The Dictaphone had been stopped due to a participant requesting a call back to start the interview, as they were not quite ready. Unfortunately, the record button was not pressed firmly enough, twice, by the researcher to re-engage the recording. Only the first three to five minutes of audio were lost, and the interview restarted when the error was realised. While there were concerns that some data would be missing, due to comprehensive note taking by the researcher the matters originally discussed were covered a second time. To prevent recording error with subsequent recordings, the original Dictaphone was replaced with a newer model that was easier to re-engage.

5.9 Data Analysis

All interviews were transcribed verbatim by the researcher using Dragon Professional Individual voice recognition software (Version 10, Nuance Communications, Burlington Massachusetts); the researcher vocally dictated back the audio from each recording into a headset. The software dictated each line of transcript into Microsoft Word. This allowed for a more accurate and less labour-intensive method compared to typing by hand, as voice recognition resulted in fewer typing corrections and equal capability when inserting punctuation (such as pauses or ellipses '…' for example). The transcripts were double-checked for accuracy against the audio before being imported into NVivo 10 (QSR International, Melbourne, Australia). This software allowed a better, more efficient overview of the data, and allowed full and equal attention to each data item, whilst also ensuring that no item was missed out (Braun and Clarke, 2006).

The data was analysed using inductive thematic analysis (TA) as outlined by Braun and Clarke (2006). Inductive TA is a very flexible method of analysis that allows for a broad focus on meaning across a dataset, and as a result is particularly suited to exploratory study (Braun and Clarke, 2013a). Braun and Clarke's (2006) guide to thematic analysis was used to analyse the data. In the first phase, each transcript was read and re-read for the researcher to familiarise themselves with the data. Initial codes were actively created by the researcher and data allocated. Next, once all the data had been initially coded and organised, the codes were revised and re-organised into themes (Braun and Clarke, 2006). Different codes were combined to form themes, and this process revisited and revised, with some irrelevant and minor codes discarded, while others were promoted to overarching themes.

5.9.1 Rationale for using inductive thematic analysis

Thematic analysis (TA) can be used to identify themes in either an inductive, or "bottom up" approach, or a deductive "top-down" technique (Braun and Clarke, 2013b).

Inductive thematic analysis (ITA) was chosen due to its 'bottom-up' research-led direction, as opposed to a theoretical 'top-down' method. By using an inductive approach, this ensured that the themes identified were strongly linked to the data themselves; the researcher attempted to make sense of the data without imposing any pre-existing expectations on the phenomenon under study (Patton, 1990). The researcher endeavoured to code and understand the relationships between the data without making prior assumptions or to fit it into an overarching theme or framework (Crabtree and Miller, 2000, Patton, 1990). This method was chosen for the analysis as it was data-driven, and the chance to openly examine participants' experiences without an overarching theoretical component or framework driving the analysis made this method a suitable choice. In addition, a further advantage of ITA is that the perspectives of different research participants, and the similarities and differences between them, can be explored across the whole data set (Braun and Clarke, 2006, Cassel and Symon, 2014).This was particularly important, due to the broad range of participants' experiences, coping strategies, and also the chance to

explore the resulting psychosocial impact on a more diverse sample of participants whose voices had not been heard in JHS/EDS-HT research before.

A second decision was whether to identify themes at a semantic, explicit level, or a latent, interpretative level (Braun and Clarke, 2006). Semantic themes are identified within the evident, surface meaning of the data, where the researcher is not looking for anything beyond what has been said (Braun and Clarke, 2006). Latent themes go beyond descriptive semantic themes to highlight the broader underlying meaning of each theme, often in relation to previous literature (Patton, 1990). By exploring latent themes, this gave a valuable opportunity, both to evaluate the results of this research and position the findings in relation to current literature. For the present phase of research, semantic or 'manifest' coding was chosen as these codes are inductive, grounded in the data, and prioritise the meanings within the data (Braun and Clarke, 2013a). This fit well with the inductive and data-driven nature of the research, and enabled the data to remain close to participants original content and meaning.

Braun and Clarke (2006) also stipulate that the ITA researcher should specify clearly their theoretical orientation, in order to permit the reader to understand the analysis and consider alternative interpretations. To explore the impact of JHS/EDS-HT in detail, a pragmatic epistemological position was deemed necessary in order to understand the challenges of coping with a chronic condition from the perspective of the participants. While as researchers we can identify the lived experience of participants, it is imperative to recognise that this experience is multi-layered (Alvesson and Skˆldberg, 2018). The way in which individuals attach meaning to experiences, and how external factors such as social constructs or gender roles interact with those meanings contribute to the multifaceted layering of reality (Braun & Clarke, 2006; 2013).

Pragmatists do not commit to any single philosophical standpoint or reality, encouraging the use of multiple worldviews or paradigms (beliefs and assumptions) to address research questions (Braun and Clarke, 2006). Pragmatism draws on a range of ideas, including employing a variety of diverse approaches and valuing both objective and subjective knowledge (Braun and Clarke, 2006). By adopting a pragmatic epistemological position, this offered a practical, realistic alternative to a

separate quantitative or qualitative approach alone (Tashakkori and Teddlie, 2003). Pragmatism uses several approaches to answer the research questions posed and recognises the benefits of using multiple perspectives to comprehend a phenomenon. With pragmatism, knowledge is gained through action and interaction (Biesta, 2009). As inductive TA is not constrained by any particular epistemology it was a fitting choice for this mixed methods study (Braun and Clarke, 2006). Therefore, by choosing a pragmatic mixed-methods methodology, both quantitative and qualitative approaches could be used to access multiple truths and meanings, ensuring a range of explanations for understanding the results (Johnson and Onwuegbuzie, 2004).

5.9.2 Rigour

Two authors (SB and SP) independently assessed the quality of the final manuscript using the consolidated criteria for reporting qualitative research (COREQ) frame-work; a 32-item checklist for reporting interviews and focus groups (Tong *et al.*, 2007).

5.10 Thematic Analysis: Findings

Five overarching themes were identified through analysis of the interview data. The five main themes are:

- Theme 1: A restricted life
  Symptom and mobility restrictions
  Relying on others
  Work and education

- Theme 2: Healthcare limitations
  Lack of awareness of JHS/EDS-HT
  Just bendy joints
  Limitations of current treatment

Difficulties with local anaesthetics

- Theme 3: Social stigma

  Judgements of others

  Hiding symptoms from others

  Looking young, feeling old

  Difficulty keeping up

- Theme 4: Fear of the unknown

  Planning ahead

  Fears of future decline

  A lack of psychological support

- Theme 5: Ways of coping:

  Psychosocial & cognitive:

  - *Acceptance*
  - *'It could be worse'*
  - *Social support*

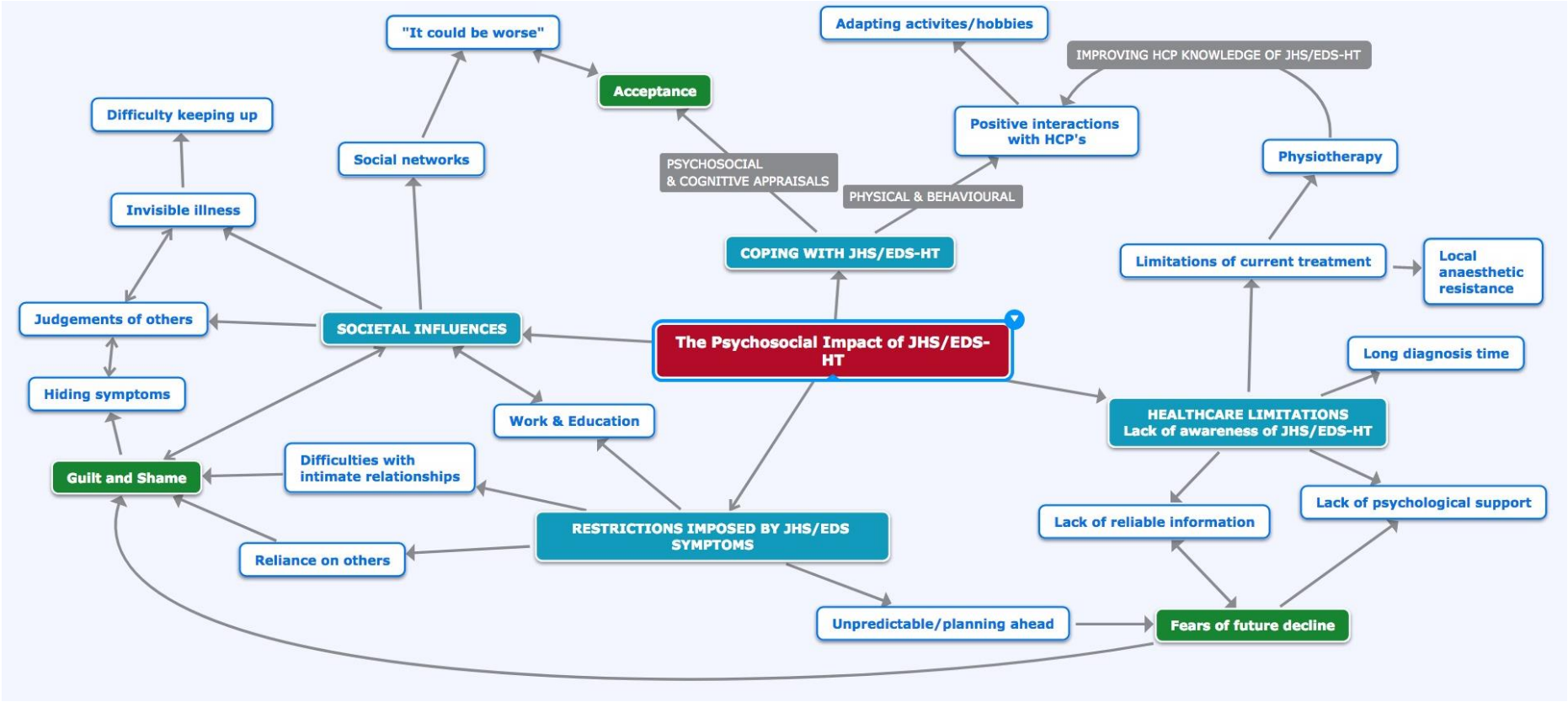
  Physical and Behavioural:

  - *Hobbies and projects*
  - *Positive interactions with healthcare professionals*

Each of the 19 subthemes are indicated by italicised sub-headings. A detailed overview of connections between themes and subthemes is outlined in Figure 5C below. All names, place names and identifying information were removed during transcription and names quoted are pseudonyms.

Figure 5C: Thematic Map

Overview of themes and how they interrelate. Abbreviations: EDS-HT: Ehlers-Danlos Syndrome (Hypermobility Type), HCPs: Healthcare professionals, JHS: Joint Hypermobility Syndrome.



The thematic map presented above (Figure 5C) offers a detailed summary of the interrelation between themes, and the number of factors influencing the psychosocial impact of JHS/EDS-HT. The map provides a broad overview of the connections between each of the overarching themes and subthemes within the interview data. Branches from the main central hub indicate the various potential influences on the participant with JHS/EDS-HT, from restrictions imposed by symptoms, healthcare-related limitations, societal influences including stigma, and coping with JHS/EDS-HT. Illustrative quotes representative of each theme are presented below. Headed arrows indicate links between themes and subthemes.

Participants with JHS/EDS-HT experienced numerous restrictions to their lives as a result of their symptoms, and of the unpredictable nature of their condition. This led to participants becoming reliant on others and could result in feelings of guilt and shame. There were a number of societal influences on participants, however those with JHS/EDS-HT faced judgements from others who did not understand the invisible nature of their condition. Although social groups could be difficult to navigate, participants tended to be friends with -and compare themselves to- others with the same or similar conditions. Participants also experienced very long waits for diagnosis, and a lack of understanding and knowledge of the condition from healthcare professionals. A scarcity of information and dependable support for their condition led some to be very fearful of future declines in their ability, and some catastrophized and panicked when faced with new symptoms. In terms of coping, participants used self-sourced information, social comparisons and social support to better manage the psychosocial impact of the condition. To manage the physical and behavioural aspects, many actively adapted their hobbies and sports to better achieve their goals, citing knowledgeable healthcare professionals as helping them to achieve this.

5.11 Theme 1: A Restricted Life

5.11.1 Symptom and mobility restrictions

Participants experienced a wide range of symptoms including joint pain and instability, fatigue, gastrointestinal issues, autonomic dysfunction (such as Postural Orthostatic Tachycardia Syndrome, which causes tachycardia in response to movement), poor circulation, frequent dislocations and injuries including Achilles tendonitis and plantar fasciitis, nerve pain, issues with bladder control, easy bruising, skin tearing and dental decay.

Dislocations were described as being very common for some participants, while others had experienced numerous partial dislocations (termed subluxations), but never a full dislocation. For those that did regularly dislocate, the patellae, shoulders, jaw and hips were cited as the most often dislocated, but potentially any joint was at risk. Of those who did dislocate, this could be numerous times a day (underlined words are emphasised in speech):

> "On a good day I'd say it's probably about ten to fifteen in a day. On an average day I'd say is probably a bit more like twenty, twenty-five? Something like that? Up to like, forty… Erm, in particular knees, shoulders, elbows ... Wrists. But yeah, it is anything really (laughs) just-just different every day, isn't it? (Exhales) so yeah, <u>that</u> every day."

[Wendy, Interview 015]

> "Dislocations, again I get a lot as well. Sometimes about ... Six a day? … Usually kneecaps, but also my left shoulder as well."

[Jackie, Interview 017]

Often a subluxation or dislocation did not take a great deal of external force. Participants had to be very careful of their movements to avoid accidentally dislocating a joint:

> "I dislocated my knee reading a magazine? Just sitting down? So have to be really careful of like the posture and the positions that I sit in?"
>
> [Bryn, Interview 011]

> "Yeah, my shoulders are pretty unstable, so my movements have to be quite deliberate, I actually have to think quite carefully about keeping my shoulders in place."
>
> [Mandy, Interview 016]

Gastrointestinal and urinary problems were cited as having a significant impact on participants' lives. Bryn's oesophageal dysmotility -a dysfunction of the oesophageal muscles that regulate swallowing- was thought to be related to her EDS-HT, and had become significantly worse on becoming pregnant:

> "Yeah, so basically, muscles and everything in the oesophagus are not pushing the food down? So get [sic] stuck? … it's really uncomfortable… I don't want to go out because I can't eat and drink, so I just eat or drink when I'm at home, so near the toilet, so if I need to go and be sick I can. If I'm at uni all day … it's quite difficult really, to stay focused, when I can't even have a sip of water all day."
>
> [Bryn, Interview 011]

Understandably, these difficulties were very disrupting, limiting Bryn's ability to leave the house and affecting her ability to socialise and do everyday things:

> "Obviously, as I'm having, er-problems eating, so I can go out for a meal, so there's a lot of activities that are ... Normal that I can't do because of my EDS, so does affect what I can and can't do."

[Bryn, Interview 011]

While treatments such as nasogastric tubes, tube feedings and drugs to alter digestion contractions could help with dysmotility problems, as Jackie found, the results of such drugs could be hard to predict:

> "My bowels stopped working in two thousand and fourteen, or fifteen? … The only problem is that sometimes the drug can work too well? (Laughs) … Or doesn't work at all, so I end up (amused) either constipated or diarrhoea, so that's nice!"

[Jackie, Interview 017]

> "Yeah, I get that, it's like I can't hold my bladder… I can't hold it, it's so painful ... I have to go to the toilet, otherwise I'm not going to make it to the toilet."

[Frances, Interview 009]

Some participants also reported difficulties with sex and intimate relationships. These problems seemed to stem from several issues. For men, the exhaustion and fatigue associated with JHS/EDS-HT made sex difficult and could lead to problems with erectile dysfunction:

> "[JHS/EDS-HT] generally makes intimate relationships more difficult[. .] For a number of reasons… 'Cause if you're exhausted and in pain all the time […] it's not happening'. And, it's very difficult for me to talk about things like erectile dysfunction."

[Jake, Interview 002]

> "It's also affected our sex life?... That's (exhales) it's not the best, to be honest, just because I'm always so tired, or I'm aching somewhere, you can't really get in the mood…Everything you do you're thinking about it."

[Nigel, Interview 005]

For affected participants, these difficulties led to great anxiety and worry regarding their relationships with their partners. Nigel was very concerned about the consequences of his sexual difficulties, and his worth to his partner, speculating whether she would be as understanding of his struggles in the future:

> "So, that's had a big effect, luckily Samantha is understanding, but it does worry me, because, you know? Is she going to be understanding the rest of ... The rest of our time together? … It's a big thing, not having, sort of, you know, the sexual side of a relationship…"

[Nigel, Interview 005]

Although Nigel was not embarrassed to bring these problems to his GP, he did not believe that there was anything healthcare professionals could do, and that his difficulties relating to fatigue and sex were just an inevitable part of many restrictions imposed by JHS/EDS-HT:

> "I mean, I've- I'd quite happily speak to a doctor, I'm not really embarrassed by this sort of thing, but … There's nothing the doctors going to be able to do with that. You know? Unless he can cure me, it's ... Just part and parcel of everything else ... So, I don't think it would be worth speaking to a health professional, to say, 'Oh yeah, we only have sex once a fortnight?' ... Because of- you know, there would be nothing they could do, would they?"

[Nigel, Interview 005]

For women, the gynaecological complications of JHS/EDS-HT could have a similarly devastating impact, particularly for Jackie, who experienced sexual difficulties after symptoms of pelvic prolapse attributed to JHS/EDS-HT:

> "It affects you gynaecological is well- …Like, what I noticed was like (laughs) your internal bits and bobs, they start to not stay with they're s'posed to be… So I was frantically doing these exercises to get everything ... back to where it was, but it's just really weird[. .] it's almost like ... Things are paralysed, and don't even ... Move properly, so you don't want anyone to come anywhere near you…The thought of it is just awful."

[Jackie, Interview 017]

Due to frequent dislocations, restricted mobility and symptoms of fatigue and pain, many participants had difficulties completing daily activities such as housework, cooking, shopping or dressing:

> "It's all I can do to get the vacuum cleaner out and then ... I'm wiped out even trying to do that."

[Lauren, Interview 006]

> "I had to portion a lot of my energy to keep myself fed properly. I have to cook, and I find food preparation very difficult, I've got lightweight pans, luckily I'm only cooking for me, you know?"

[Rachel, Interview 010]

"I don't know if you find, but I find buttons very difficult… Doing buttons up, and things like that-… just trying to keep my thumb in the same place is just- and it just doesn't want to, it wants to ... Go in a different place."

[Anna, Interview 014]

"If I get orders, parcels and such like that, I can't um, lift them, so like lifting products and things like that. I have to get someone to help me with that."

[Roger, Interview 003]

5.11.2 Relying on others

To complete the tasks that they couldn't manage, participants sometimes had to rely on their partners or family for care needs and support. However, this left them feeling guilt, shame, 'like a burden' or that they were holding family members back from living a normal life:

"That's one of the biggest negatives I have at times, if I'm having a bad night, a bad ... period in my health, or whatever, I always feel like, I feel like I'm a burden… Family-wise, [...] I feel like a burden to [Wife]… 'Cause obviously, like- when my wife has to, like, she looks after me and helps look after me- And, I feel sometimes like I'm restricting her."

[Roger, Interview 003]

"I had a massive freakout at my partner on holiday, like, 'I'm holding you back in life.', He's always like, 'That's not true at all, shut up, it's fine, come on, let's have a cuddle."

[Frances, Interview 009]

> "The impact it has on relationships, I feel like I'm holding my husband back from having a normal family life?"
>
> [Anna, Interview 014]

Sometimes, the need to look after their partner caused obvious resentment in the family members of participants with JHS/EDS-HT:

> "My husband used to do stuff like that for me, but he used to get really angry and ... So, he cleaned the house for me but he'd throw things, and crash things, and um, smashed the place up because he'd get angry […] that it was all on him."
>
> [Lauren, Interview 006]

Over time, worries about their household responsibilities, holding their family back and being a burden could lead to exacerbations of anxiety and depression:

> "Sometimes I feel a burden, or a nuisance […] I go into myself? Where I don't want to talk to people? […] Somedays I'll like, I won't talk about my problems, even to my wife […] that's why I end up erm, having the anxiety problems. And that's why I end up having to see a counsellor and such.… And like- like I say, with the depression, it kind of ... it's not really feeling sorry for myself 'cause I never really feel sorry for myself? But it's like, feeling sorry for other people, having to put up with me?"
>
> [Roger, Interview 003]

> "That does get me down, that I ... Can't help around the house as much as I should, for I feel I should."
>
> [Nigel, Interview 005]

> "And it makes me feel a bit ... Like sad? Seeing younger siblings do things for me?"
>
> [Emily, Interview 007]

> "In terms of my husband, I feel he's not having ... A fulfilled lifestyle […] like the past couple of days, he's had to take care of me. And ... I don't think that that's healthy. So that ... Affect my confidence, and the way I feel about myself."
>
> [Anna, Interview 014]

In cases where the symptoms of anxiety and depression had seemed to overwhelm participants, many had sought the support of their GP, who had arranged medication and counselling for those most severely affected.

5.11.3 Work life and education

Participants also faced restrictions to their work lives and education due to the symptoms of JHS/EDS-HT. Some spoke of being bullied and humiliated by classmates for being physically different from their peers. Others had difficulties holding pens with hypermobile fingers and writing for any length of time. Due to a lack of understanding, Anna's teachers had presumed she was being lazy, rather than experiencing pain:

> "Your fingers extend too far? So holding the pen's quite difficult…they just presumed I was being quite lazy, like, you know, because I used to stop writing, and because it used to hurt so much, and they used to say, 'Come on, you have to finish your work'. They'd keep me in at break, I was actually punished for not finishing my work. you know, I was genuinely in tears some days."
>
> [Anna, Interview 014]

The majority of participants had started their work lives without a diagnosis of JHS/EDS-HT. Many had initially worked in roles that were not suited to their condition, involving standing for long periods, working in cold weather and heavy lifting, which soon led to flare ups of symptoms:

> "I had a lot of problems with my feet, because you're standing up all day… you're walking all day and you never stop… I could have had them amputated they were hurting so much."

[Nigel, Interview 003]

> "Because I was sitting down all day, hunched over a microscope. I was aching a lot, so I left there."

[Nigel, Interview 003]

> "I was getting frequent injuries, and not really picking up on why…when I was told by the physiotherapist what it was, and she asked what line of work I was doing, and I told her, and she was like, 'I think you really need to rethink what you're doing.', erm, 'because it's going to just put loads more stress on the joints', you know? 'Bending and lifting such heavy things, you shouldn't be doing that."

[Anna, Interview 014]

Lauren admitted that had she been diagnosed earlier, she would never have chosen nursing as a career:

> "If I'd known that I had EDS I would never, in a million years, have gone into nursing ... It's the worst thing you can do, constant lifting and bending, and ... It killed my right shoulder, because that's the arm I always lifted with, so."

[Lauren, Interview 006]

This echoed previous research into the psychosocial impact of JHS/EDS-HT, as many participants had also been forced to limit or change their career plans due to the symptoms of JHS/EDS-HT (Berglund *et al.*, 2000). Almost all participants employed in the present study had reduced their hours in an effort to manage their pain and fatigue and to better accomplish their activities. By working reduced hours and avoiding long commutes, participants could pace their energy reserves for the week and prevent exhaustion:

> "So, reducing my hours was a big difference to me, I now work for four full days, I have Friday off so I've got an extended weekend to, y'know, recover."

[Georgina, Interview 006]

> "But I'm only able to do part time? Um, I've been told to try and ... Pace myself, a little bit more. So, rather than do five days part-time, I'm doing two and a half days. I get two rest days in between, midweek."

[Anna, Interview 014]

> "This year I've dropped down to 4 days, so I can Wednesday off? Which is making things a lot easier in terms of pacing ... two days on, day off, and then back in Thursday, Friday. Um, that's much more manageable."

[Mandy, Interview 016]

> "I was finding that by the time I get to the weekend I spend all weekend recovering from my commute and stuff, so then it's just wasted. So my work are really good, and said, 'Well, have a Friday working from home, so you don't end up wasting your weekend, you've still got that work-life balance.'"

[Wendy, Interview 015]

Others had set up their own businesses at home. Roger's online company gave him the flexibility to work hospital appointments and flare ups in symptoms around his job:

> "So I realised that I needed to do something that I was more accessible at doing…. I can work from home, I can deal with all my orders and stuff. I 've- my wife helps as well…If I'm having a bad day I don't put as much in, or if I'm having a good day I'll do more work on my website […]I can't always do as much as I would like."

[Roger, Interview 003]

Despite making accommodations, Roger's comment that '*I can't always do as much as I would like*' reiterates his longing to be able to do more, and the restriction imposed by JHS/EDS-HT. The majority of participants had very supportive workplace environments with accommodations and modifications made to allow them to keep working. These included laptops allowing them to work from home, automatic door openers, modifications for wheelchair access and consideration given to participant's mobility needs when rooms were booked for meetings. Since being diagnosed, Georgina had encountered a great deal more support from her manager:

> "My manager's pretty flexible with me. I tend to, sort of not book any of my support time until ten, eleven in the morning? So, if I'm having a crap morning I'm going a little bit later, make my time up later, and things like that."

[Georgina, Interview 008]

Working was important to participants, even if they did not get paid as much as they would like, as they felt that work gave them a role in society and a purpose in life, which in turn benefited their emotional wellbeing "*Even if I don't get ... any money*

or anything, at least I'm doing something useful" [Rachel, Interview 010]. Anna emphasised the need to stay positive, despite the potential restrictions to working for those with JHS/EDS-HT:

> "I'm trying to keep myself working, I know quite a few people who would just give up, and try and get the benefits that they're entitled to, things like that, which is great for them, but for my wellbeing I feel that I need to be doing something…So I try to keep working, just to give me ... another four walls, away from home, to try and keep myself positive"
>
> *[Anna, Interview 014]*

5.12 Theme 2: Healthcare limitations

5.12.1 Lack of awareness of JHS/EDS-HT

Every participant interviewed reported an overall lack of awareness of hypermobility syndromes such as JHS/EDS-HT among healthcare professionals, including consultants, GPs, nurses and physiotherapists. This naturally resulted in patients taking many years to be diagnosed:

> "That was around ... two years ago, and I've had symptoms from when I was five…So, I had thirty-five years undiagnosed."
>
> [Nigel, Interview 005]

> "I was ... Forty? Forty-one? Yeah, but it's only been the last four or five years that it got progressively worse, to the point that I thought, 'Well, there's something wrong with me.', Rather than just, 'I'm very unfit.', Or whatever."
>
> [Georgina, Interview 008]

> "But I was ... Fifty-five… but it was quite by accident, but we've been going to the same GP for, you know ... Twenty, twenty-five years?"

[Rachel, Interview 010]

> "So was from the age of eleven, (sigh) but it was twenty-three when I got the diagnosis! (Laughs)… Er, there just wasn't the awareness I don't think. Of what it was."

[Bryn, Interview 011]

As a result of extensive investigations, referrals to numerous secondary care specialties and in light of repeatedly normal test results, many were told for years that nothing was wrong. Anna was finally diagnosed aged 39:

> "So, I had to have an MRI scan and nothing showed up, so they sent me to haematologist, who did blood tests, nothing showed up, and that's when they referred me to a rheumatologist, and that's when I was diagnosed, and that was in ... Two thousand and thirteen? -And that was obviously quite a time, so I've gone all my life, up to that point, with the symptoms and been told, there's nothing wrong with me."

[Anna, Interview 014]

Others were labelled hypochondriacs, accused of exaggerating, or told that their symptoms were 'all in their head':

> "'Don't think there's anything wrong with her.' you know? 'She's just making it up.'"

[Rachel, Interview 010]

"Doctors told me, 'You're making it up' because there's no way I can get dislocations?"

[Bryn, Interview 011]

"I've seen that so much, people who've got…anything that's medically unexplained, um, the doctors- in front of patients, and in private, will be like, 'Well, there's nothing wrong with them, they're just making it up. It's all in their head.'"

[Frances, Interview 009]

"But, I've spent several years going back and forward to doctors, having them tell me, 'It's all in my head', 'It's all my imagination', and this, that, and t'other."

[Georgina, Interview 008]

"I used to get called a hypochondriac a lot, and um, yeah and got told I probably had some kind of mental health issue! (laughs) Or, er, all manner of things!"

[Jackie, Interview 017]

When injured, joints naturally lose their range of motion, becoming swollen, stiff and difficult to move due to a build-up of fluid. Conversely, the extreme flexibility and joint range of motion typical of JHS/EDS-HT, even in the case of pain, was often mistakenly attributed as a sign of fitness by healthcare professionals:

"[Doctor:] Can you bend over, touch your toes?', 'Yeah?', 'Well, then there can't be too much wrong with you.'"

[Tabitha, Interview 012]

Patients reported that Fibromyalgia, a commonly co-occurring diagnosis in 29.4% of this study cohort, could also be viewed negatively by some healthcare professionals:

> "Doctors regularly refer to it as a fake condition, and like obviously not in public, but in private they'll be like, 'Oh, it's not real,' or, 'Oh, it's a middle-class syndrome for people who don't want to work,' you know? And ... It's really horrible, and when you hear it you're like, 'Wow', and, you try and say something like, 'I really don't think it is,', 'Oh no, definitely, you haven't seen enough. It's just people making it up who don't want to work.' […] And these are people who can be perfectly nice to patients ... As soon as the patient's gone, they're like, 'Y'know, they don't really have anything wrong with them. It just makes them feel better if you pretend they do.'"

[Frances, Interview 009]

Unlike JHS/EDS-HT, the underlying causes of Fibromyalgia have long been debated within medical literature. While there is considerable interest in finding an absolute cause, none have been established as a valid explanation, which has led to scepticism surrounding the legitimacy of Fibromyalgia as a medical disease (Looper and Kirmayer, 2004). To prevent being disregarded by healthcare professionals, Anna, another participant with both JHS/EDS-HT and Fibromyalgia, was encouraged by her physiotherapist to disclose her hypermobility to doctors first, in order to avoid dismissive reactions:

> "They don't really think that ... Fibromyalgia is a thing? And um, even the physiotherapist said, 'If anyone asks what's wrong with you, say the hypermobility first, don't say that you have Fibromyalgia and hypermobility, because […] as soon as they hear Fibromyalgia they shut off.'"

[Anna, Interview 014]

In the face of continuous disbelief and sceptical remarks from healthcare professionals, Nigel and Frances started to doubt their own judgments about their pain sensations:

> "Until you get diagnosed just feels like ... you know? 'Am I really aching?[. .] there's nothing wrong with me I've had all the tests for arthritis and they will come back negative, tests for this, tests for that, and that's all negative, maybe it is all in my head?"

[Nigel, Interview 005]

After many instances of being mislabelled as hypochondriacs, several participants described their eventual diagnosis as a very positive experience, as years of symptoms were finally given a recognised cause:

> "I used to think I was a bit of a hypochondriac, to be honest! But er ... No, it all makes sense now… it was actually reassuring, is when you realise you're not going mad!"

[Claire, Interview 013]

> "It's just- it all makes sense? I'm not a hypochondriac, I'm not imagining stuff, this is- there's a reason for these things. And it takes a little bit of, I don't know? Pressure off, in a way. This is just- ... Okay, that's how it is. And that's the reason for these things."

[Mandy, Interview 016]

> "It- it was a relief, because finally, FINALLY! (Laughs) I could see, 'Oh my God?' Once you saw that all these symptoms are part of EDS, and that Fibromyalgia and EDS were very common and went together-"

[Lauren, Interview 006]

Being given a label of JHS/EDS-HT enabled participants some degree of vindication, after having their credibility called into question over many years.

5.12.2 Just bendy joints

However, even with a verified diagnosis, some felt that their symptoms were still dismissed by healthcare professionals as, 'just bendy joints', rather than seeing the wider psychosocial impact of the condition on participants' lives:

> "The first consultant I went to see, 'Yeah, you're just bendy, don't worry about it.'"

[Frances, Interview 009]

> "'That's bendy joints, I don't need to know about that', he was really dismissive."

[Mandy, Interview 016]

Later, Mandy reflected on whether her consultant's attitude was due to a lack of understanding about JHS/EDS-HT:

> "I think even with medics, even if they've heard of EDS, it's misunderstood. They often ... are, 'Oh yes, I've heard of that ... Yeah, you got bendy joints' And it sort of, full stop. And it's like, 'Yeah, but there's a bit more to it than that!' (Exhales) and they- they can find that quite hard."

[Mandy, Interview 016]

Almost all participants gave examples of healthcare professionals' negative reactions and attitudes, such as becoming angry or being dismissive of their symptoms. Others

spoke of feeling objectified during medical examinations, with their hypermobility treated as a spectacle to be regarded:

> "And then he was like, 'Wow! You're such a freakshow!', and I'm like ... 'Wow. Not a nice thing to say, thanks!' … but, I think there's definitely that, 'Ooh, let's get all the medical students here and show them!' And I'm like, 'No, you cannot bring the medical students here and show them, no!'"

[Frances, Interview 009]

Jake speculated whether some doctors' negative reactions could be due to the biomedical training they had received, with its emphasis on '*fixing*', combined with inherent frustrations regarding the chronicity of JHS/EDS-HT:

> "So I try and remember that, especially with doctors whose WHOLE kind of, unconscious raison d'être for being a doctor is, "I. Make. People. Better."… And then you provide them with an incurable condition![. .] And they're like, "Just get out of my surgery and stop making me feel inadequate!"… Yep. And people with chronic pain, of course, you can't fix. So. (laughs)"

[Jake, Interview 002]

5.12.3 Limitations of current treatment

Having been given physiotherapy exercises that made their joint pain worse was a commonly reported outcome, and it was suggested that not all physiotherapists had the specialist knowledge to adequately identify and treat JHS/EDS-HT. Rhiannon's physiotherapist had failed to notice her hypermobile joints:

> "[The physiotherapist] wasn't able to see that my joints over-stretched. And she gave me lots of stretching exercises and it kind of- it really really crippled me […] I would (laughing) say that really put me off, actually!"

[Rhiannon, Interview 001]

Participants struggled to remember their exercises and compete them correctly at home:

> "I went to the first appointment and we spent all that time talking, and then the end she ran through ... Three or four exercises in about half a second, and I was just like I never caught any of that, then she didn't like to see me again so I was like what is the point?"

[Dana, Interview 004]

These problems may be due to the impaired proprioception associated with JHS/EDS-HT (Castori, 2012, Terry *et al.*, 2015). Proprioception (from the Latin *proprious*, meaning "one's own" and *perception*) refers to the 'perception of one's own self', a sense of one's own body in space, including a sense of limb movement and position (Hillier *et al.*, 2015). Participants with poor proprioception can experience problems locating their limbs in space when they are not looking at them; '*I lay on my back, and I don't know where anything is* [Roger, Interview 003]. As Claire describes:

> "I've got no spatial awareness, if someone says to me, 'Your knees are bent', I have to say, 'Were they?', Unless I can physically see myself, I don't even know that one leg is straight, one leg's bent."

[Claire, Interveiw 013]

> "At times, I don't always know when my joints are, I don't have ... The greatest ... um sense, of them being in place, you know? Sometimes…my legs will be really awkwardly wrapped, and I don't really realise that it's not ... Normal? … Sometimes, if I do physio exercises at home, it's like I'm not doing the movement right at all, but I can't tell I'm not doing it right, so if I'm in front of a

mirror, I could be going through the motions but I'm not ... Actually doing it correctly."

[Frances, Interview 009]

5.12.4 Difficulties with local anaesthetics

A significant number of participants described instances where local anaesthetics such as Lidocaine had been ineffective, thought to be due to the underlying collagen defect present in JHS/EDS-HT (Wiesmann *et al.*, 2014). This can result in patients undergoing surgical and dental procedures fully aware of pain:

"I've had a root canal, previously, and the local anaesthetic has not worked at all? … And, I'll be there ... Crying, and they're like, 'I've already put in more anaesthetic than I should do already, I'm really sorry, I can't give you any more.'"

[Frances, Interview 009]

Even though Mandy, Jake and Nigel spoke up, their complaints of pain were not taken seriously:

"And it was OK to start with ... but very quickly I could feel what they were doing. And I- I spoke up, and ... [the doctor] basically said, 'No, you can't.' and carried on. Um, but I was in a lot of pain?"

[Mandy, Interview 016]

"I had minor surgery done, which is, I don't know if you know the first cut of a facelift? […] inside the ear going down along the jawline… They start poking me and I'm like, 'I can still feel that'. Doctor becomes ... very, very irritated… Packs it full of Lidocaine again, and cuts?"

[Jake, Interview 002]

> "The anaesthetic didn't work, so ... They injected into my calf…. They cut through the first layer of skin, and I felt it… So, this stopped, put some more anaesthetic in, went to the next layer below, give a five or ten minutes, 'Can you feel that now?', 'Oh no, that's fine.' Cut me again, I felt it again, so by the time they got to my calf to cut the- the fibre away-… I'd felt it all."

[Nigel, Interview 005]

Having experienced painful procedures in the past, and recognising the potential link between JHS/EDS-HT and anaesthetic resistance, Nigel and Bryn had both made attempts to warn their surgeons during subsequent procedures, but to little success:

> "'Right, one of the symptoms of this Ehlers-Danlos is that anaesthetics don't always work and I felt it last time?' and the surgeon said, 'What's Ehlers-Danlos?'"

[Nigel, Interview 005]

> "They [had] no idea when I was having the operation about the anaesthetic effects of EDS […] just looked at me a bit, like I'm making it up!"

[Bryn, Interview 011]

> "You have to try and explain to them, 'I'm not a junkie, I'm not saying that I ... Want all this extra stuff, because I want to get off my face! (Amused) I'm saying it because the normal stuff ... Doesn't work on me!"

[Jackie, Interview 017]

Again, participants described encountering a lack of awareness of JHS/EDS-HT. After multiple attempts to evade pain to no success, participants seemed resigned to their fate, citing a determination to '*just get on with it'*:

> "[On experiencing pain awareness during a dental procedure] *I'm like, 'It's okay, carry on."*
>
> [Frances, Interview 009]

> "Um, it's quite horrific to speak about, but obviously, having children I had to have a local anaesthetic for a um- ... They had to cut me, to get the baby out?[. .] And they just- they expected it to work and didn't? Um, so. Yeah. Quite an experience, for them more than me, because I just- I just got on with it! (Laughs)"
>
> [Anna, Interview 014]

Others had been injured by staff who did not take their warnings regarding dislocations seriously. Bryn describes a disastrous trip to her GP who did not believe her risk of dislocation:

> "He's even ... Dislocated my hip, because he told me it can't happen? So he pulled on it and it come out the socket…He just gave me the tissues after, and I was in agony."
>
> [Bryn, Interview 011]

> "Oh God! The physio! Jesus ... um, so the physio… just didn't know what I was talking about… when I said about the fact that my kneecaps dislocate, they look to me like I was mad, and then said, 'Oh, let's just have a look at them', and then both of them dislocated my kneecaps, with their hands-…And then went, 'AAAAAHHH!', I thought, 'You're screaming? I'm the one who just pushed my

kneecap out!' And they were like, '(gasps) Oh my god! They actually do dislocate don't they!?'"

[Jackie, Interview 017]

A combination of dismissive attitudes from healthcare professionals, and a lack of treatment options had made Rachel wary of asking for any more medical intervention:

"I can't even be bothered to tell anybody about it, because I just don't want any more intervention, I just want to keep away from doctors if I can, if it's desperate I'll go see them, but unless its desperate I won't bother because (exhales) I don't know? …It just seems like ... You know, it's just, 'Oh, well, we can do this but it doesn't really help? […] So, I think while I'm still living, breathing, and talking, I'll just ... Get on with it! You know?"

[Rachel, Interview 010]

5.13 Theme 3: Social Stigma

5.13.1 Judgements of others

Due to the invisible nature of JHS/EDS participants often faced judgements, from strangers, friends and other disabled people. Confrontations typically occurred when using assistance designed for people with disabilities:

"People'll… look at me and say, 'Well, why have you got a disability badge?'

[Roger, Interview 003]

> "I've also gotten abuse off of disabled people? Because I've got a blue badge, and I got abused several times from ... Disabled people, for all saying to me, 'Oh, why are you parking in a blue badge space?'
>
> [Jackie, Interview 017]

> "And they're like, 'Yes?' and I'm like, 'Wheelchair assistance?', 'Oh, really?'… 'No! I just thought it'd be fun to make it up at the boarding bay!' You know what I mean? …And then you have to explain what your condition is. In front of the entire queue [. .] because you look fine"
>
> [Jake, Interview 002]

Participants mentioned '*looking well'*, '*looking young'* or '*looking fine'* as potential reasons why they had been stopped. Participants described feelings of embarrassment, guilt and shame when confronted by others, even though they had an equal right to use the accommodations. Mandy questioned whether this judgement was due to those with JHS/EDS-HT not fitting the perceived notion of disability as a visible difference:

> "But, other people's judgement. Just ... because so may people have this like, ... Schema? Don't they? Of what, in their head, is disabled. And if you don't fit that ... Notion of what disabled is in their head, then they get really confused."
>
> [Mandy, Interview 016]

Some wondered whether their JHS/EDS-HT would be easier to understand and more readily accepted by others if signs of the condition were more visible:

> "I'll be honest with you, quite a lot I actually wish I was in a wheelchair! Do you know what I mean? I just feel like ... People can understand that?"

[Jackie, Interview 017]

> "If I was in a wheelchair… They'd be like "Oh, poor man" ...…And they'd be less inclined to be assholes about it."

[Jake, Interview 002]

Others used a walking stick, cane or crutch to make it clear to other people that they required help:

> "Even if I can walk all day I keep my folding walking stick with me at all times, so if I'm on public transport I take it out so people have that visual ... cue, that if I asked them to sit down, I'm not just making it up, and I do need a seat."

[Emily, Interview 007]

> "I actually carry my stick with me?[. .] I have to use that to make it clear I have problems… Which is a shame… they actually look at me and think, 'Here, cripple, have a seat.', or, 'Let's get you on the plane first,'"

[Claire, Interview 013]

Numerous participants found the invisible nature of their condition an asset:

> 'Because people don't see it, and people wouldn't know unless I told them, they don't see me as ... like the illness if that makes sense?'.

[Rhiannon, Interview 001]

> "I definitely don't want to be defined by my Ehlers-Danlos Syndrome, like ... I prefer not to let people know. It's better ... That it's hidden in that sense."

[Emily, Interview 007]

Here, Rhiannon and Emily are both open to the fact that by not being a visible difference, they are not 'defined' by their disability. Similarly, Jake felt that he could '*choose how and when I bring up my disability*' [Interview 002]. Described by Charmaz (1997) as protective disclosing, choosing how, what and when to tell others about their condition affords participants a sense of control. Although the ability to hide disability may seem like an asset, invisible differences literature has indicated that the effort of maintaining a hidden difference can be psychologically stressful, due to the fears of being rejected, stigmatised, and potentially experiencing problems with the responses of others (Charmaz, 1997).

5.13.2 Hiding symptoms from others

Fears of being judged led many to hide their symptoms, in an effort to "*pretend it's okay*" [Nigel, Interview 005]. Participants felt psychologically invalidated, expressing hesitancy in being perceived as a 'faker' or 'someone who always complains':

> "[People] think you're exaggerating. Or that you're, possibly even ... Faking things? I don't know, but obviously from my perspective, it's the opposite, I actually think well, I'm trying to hide how much pain I'm in, rather than overdo it."

[Jackie, Interview 017]

> "I hide it. I try and hide it. I- I don't- (exhale)[. .]'cause like using my braces and such they're under my clothes, but unless they see me in my wheelchair they don't see any problems, so to speak?"

[Roger, Interview 003]

> "I felt that I had to ... Try and appear normal all the time"

[Lauren, Interview 006]

This was particularly evident in Nigel's interview, where he described having to wear a '*fake mask'* at work to hide how he really felt:

> "I know I wear a lot of masks, especially at work, and if you asked any of my colleagues when I was like, they'd say, 'Oh, he's always happy,' erm, 'He's got an illness but it doesn't really affect him.' ... Because I don't show them that side of it… And everyone outside, y'know, gets the fake mask, where every day you say, 'Yeah, I'm fine how are you?'… And I'm not fine, you know? I'm in agony."

[Nigel, Interview 005]

Like Roger and Jackie, Nigel believed that other people might think negatively of him if they knew about his pain. Acknowledging their invisible difference to others took a great deal of confidence, yet some described feeling embarrassed when asking for accommodations such as a seat on a train, "*People are judging me.' and I just kind of want to ... get on quietly and I'll skulk away*" [Mandy, Interview 016]. Interestingly, Jake described having to ask strangers for a seat on a train as undermining his masculinity:

> "And I mean, this [asking for a seat on a crowded train] is the stuff that's difficult for us. Cause it does. It chips away at [you] […] I estimate that for men it's quite difficult, because they can't. Because so much of it ... chips away ... at your masculinity."

[Jake, Interview 002]

Dominant models of masculinity indicate that men are expected not to show pain, to be self-sufficient and not appear weak to others (Gibbs, 2005). Both the symptoms

of JHS/EDS-HT such as pain, fatigue and limited strength, in addition to needing to ask for assistance and depending upon others may undermine the image of strength and independence associated with masculinity (Gibbs, 2005). As a result, Jake may feel that he is being perceived in a position of marginalised masculinity (Cameron and Bernardes, 1998, Charmaz, 1995, Gibbs, 2005).

5.13.3 Looking young, feeling old

Many described the discrepancy between their healthy outward appearance to others and internal pain and exhaustion as 'looking young but feeling old':

> "I'm only twenty-seven and I feel like an eighty year old."
>
> [Wendy, Interview 015]

> "And again just frustrated I think, kind of- thinking "Well… I'm only twenty-eight"… Y'know is this just going to get worse and worse? And I'm- and I'm not exactly old."
>
> [Rhiannon, Interview 001]

> "She just goes, 'Oh, it's because I'm getting old.', And I think, 'Oh, lucky you! I'm only fourty-two!' (Laughs)"
>
> [Georgina, Interview 008]

> "…Looking younger on the outside doesn't compensate for some days feeling about a hundred and fifty on the inside."
>
> [Tabitha, Interview 012]

The dissonance between inward and outward appearance resulted in a number of participants describing feeling disconnected from their physical bodies. Rachel, for example, no longer felt that her body and mind were whole:

> "I don't know if you've ... Got this? ... You think of yourself as a whole, don't you? Your mind and body, whole?…I think very much of me, as in my brain, and my body is something that is carrying it around ... …I've got altered feeling in most of my body. And no feeling in quite a few bits, and pain in the rest (laughs) so, it's just not that attractive to me, now, you know? To my brain, being in my body isn't attractive to me… I feel very much in my mind, if you know what I mean?"

[Rachel, Interview 010]

These feelings of reduced attractiveness may be due to the altered pain and perception sensations that Rachel describes. What is noteworthy is that she then disregards her body as less attractive. These feelings may also be due to an inability to accept the changes in her body since her physical condition has declined. As Jackie describes:

> "Because this body doesn't feel like my body. I just, I literally sit there and I feel it, and I think, 'This body's flabby, this body's fat'. My body used to be tall and ... This doesn't feel like me…. The thought of it is just awful, because you hate yourself, and you don't feel like you anymore. So, it affects you in that way and- and it just takes all your self-confidence away. You don't feel like the same person, and you're not the same person. You see a photo of yourself and you think, 'That doesn't look like me' and you can't do any of the things you want to do any more. So for me, I feel like my identity has been taken away from me as well… Like that was another person?"

[Jackie, Interview 017]

Jackie and Rachel both describe their bodies as less attractive the further they stray from the younger bodies of their past. Body image is gendered, in that men and women are socialised to view their bodies in different ways, and to attribute different physical qualities and standards (Clarke *et al.*, 2008). Women, for example, are encouraged to view their body as an object to be evaluated by others (Franzoi, 1995). The ideal male body is healthy and projects an image of strength, while likewise the ideal female body is healthy, thin, shapely and young (Grogan, 2017). However, within this lies a double-standard, in that while men's aged bodies are full of 'character', older women's bodies are reviled and considered less attractive (Clarke and Korotchenko, 2011), (Clarke *et al.*, 2008).

5.13.4 Difficulty keeping up

Difficulty in keeping up with friends, family and colleagues led to feelings of frustration and anger in participants, as their joints could not always withstand what they wanted to do:

> "I think I do find it frustrating for example when I'm at bouldering if- um and I'm trying to do a particular, say- a particular route on the wall and ... my hips-, my hip or my wrists are kind of cracking as I'm trying to do it, and I just think "Agh, I can't do it" and that- that's frustrating."
>
> [Rhiannon, Interview 001]

> "Why can't I do what everybody else does? Why am I the only one who can't ... Go for this walk?' You know? 'Do this thing that everyone else is doing.', And that got me really low before the diagnosis, because I just thought I was not as strong as everybody else just not as fit, just not as capable."
>
> [Nigel, Interview 005]

Participants also described a number of internalised negative feelings about their own bodies. Some described themselves as 'freaks', experienced shame and guilt and expressed a longing to be 'normal.':

> "I guess made me (long pause 3s) a little bit? Frustrated with my body? That ... it can't be ... a bit more normal."

[Rhiannon, Interview 001]

These limitations echo Bury's (1982) finding that chronic illness can cause '*biographical disruption'* (p.167) in that the person must reassess expectations about the functioning of their body, daily activities and self-concept in light of their physical limitations, chronic pain and the resulting changes in their future options and plans (Bury, 1982), (Clarke *et al.*, 2008).

5.14 Theme 4: Fear of the unknown

5.14.1 Planning Ahead

The fluctuating nature of JHS/EDS-HT and need for accessibility required participants to continually plan ahead, whether in terms of pacing, activities outside the house, or planning movements to avoid dislocations. However, while planning ahead helped participants to better manage JHS/EDS-HT, several felt that by continually having to plan ahead they lost the freedom of spontaneity:

> "We've always got to plan where we want to be and how we want to get there? […] places that are accessible. It's that sort of thing you are planning everything more ... ahead. You can't be spontaneous."

[Roger, Interview 003]

"I think definitely planning ahead as much as possible, and yes it can mean you loose some spontaneity, some excitement, but I think that planning ahead in terms of recuperation time ... um, if you're going to do an activity. For me, I try and say to myself, 'Don't let it stop me doing anything, but make sure you've got that recuperation time in afterwards'"

[Wendy, Interview 015]

"I have little trouble with my shoulder subluxating the past few weeks, I've literally had to stop and think, about how far out I can reach my hand, or how high up I can lift it?[. .]Rather than just doing it without thinking ... And I think in some ways doing that helps, but at the same time you've lost the spontaneity."

[Tabitha, Interview 012]

5.14.2 Fears of future decline

Not knowing when the next injury was going to occur, how their illness trajectory was going to affect them over time and not knowing the potential impact of JHS/EDS-HT on their future plans made participants especially fearful of future declines in their physical ability:

"I don't know where I'm going to end up in the future, I try not to think about the future, because um, if like this now, what am I going to be like in the future?"

[Lauren, Interview 006]

"Which probably then is a bit of a cycle because ... when I'm in more pain I tend to worry more […] "Oh God, is this?- …"Is my body going to completely fall apart?" (laughs) Um. So yeah, I think I'm quite a worrier anyway?"

[Rhiannon, Interview 001]

For participants with affected parents, their parents' struggles were a vision of their own future:

> "All the things I can do now, [Mum] could do when she was my age…But now, she needs a double knee replacement because her knees are just so worn out?"
>
> [Frances, Interview 009]

Fears of future decline also linked to Roger's worries about depending on other family members, and feelings of guilt, shame and being a burden on his loved ones:

> "I still am- frightened of what the future holds, erm, how the Ehlers-Danlos is going to get worse, or how it might affect me? […] cause I know that one day I might be ... confined to my wheelchair and I might not be a- able to ... do as much for myself. And there's a limit to what I can do for myself now, so I always worried that like, one day I might not be able to do anything. And it's that fear of being a burden again?"
>
> [Roger, Interview 003]

Many participants took the initiative in finding out more about their own condition, and had joined support groups, internet forums and a variety of social media pages. However, meeting or seeing others with JHS/EDS-HT, in person and online, who were more severely affected than themselves sometimes led to a '*vicious cycle'* of fears concerning their own potential future declines in ability:

> "That's the only thing I've looked up, partly because ... I'm slightly ... wary of (laughing) stuff you find on the internet? … About illnesses. Um- and … I don't want to find some forum where people are talking about this awful stuff that's (long pause 2s) y'know, happened to them or could happen-"
>
> [Rhiannon, Interview 001]

> "Obviously with Ehlers-Danlos there's such a range of- you see one person it doesn't affect so badly and you see someone else it affects really badly?[. .] I think reading- some of the stuff on the internet, like ... it does it feeds like- it fills your head with fear in some respects. You're always like […] 'Ah they've got to be fed through a tube' and things like that. And say, I'm having problems with my stomach at the moment, and I'm like, 'Ah! I don't want to end up like that!'. It's that fear that, 'Ah, that could happen!', you start getting into a- a circle and you just- ... Like I say I just- I'm over-thinking things and then I start panicking, it's like, then it's a vicious circle."
>
> [Roger, Interview 003]

Lauren had decided that support groups were not for her, after experiencing negative attitudes from other members:

> "To be honest with you, I don't know that it's for me? I found it a bit depressing because I don't want to sit there and say, 'Oh I've got this wrong, I've got that wrong, I used to be able to do this and now I can't do that anymore.' Which is what I found other people were doing… it just kind of brings it home somehow, I get , more depressed, and I think I don't want to know."
>
> [Lauren, Interview 006]

These fears led to catastrophising responses to new or unusual symptoms, as participants became anxious as to whether the new symptom signalled their own health decline:

> "I do have a tendency to (laughs) over-analyse things! Um, so (long pause 2s) yes, I think- I think um, I think particularly when it's different pain or when it's slightly- or when it's in a new area. Or if it's in the same area but it feels different to normal? I think I get quite anxious about that because I'm kind of like, (higher) "Oh, what does this mean?" "Does this mean that it is (inhales) getting worse?"

[Rhiannon, Interview 001]

> "The problem with EDS, as you will know, is that sometimes you have a symptom and it's nothing to do with EDS! (Laughs) it's just like-, it's just some random symptom! Or maybe you're coming down with a cold, or something?[. .] And you start thinking, (amused) 'Oh, God! Is this something NEW!?'"

[Jackie, Interview 017]

Many spoke of a lack of reliable information about their condition, other than in published books and research journals. All accepted the need to gain their information about JHS/EDS-HT from reputable sources such as patient support groups, rather than "*just picking up things on forums*" [Roger, Interview 003]. However, participants recognised that not everyone with JHS/EDS-HT would have access to trustworthy information or be able to understand a research paper:

> "And I think there's a lot of… misinformation out there as well I think ... about different things…There doesn't seem to be a huge amount of research into it, or information about it, available."

[Rhiannon, Interview 001]

> "…There's a lack of information as well, I know that a lot of people with EDS have got splints or braces, and I've been trying to find out how I would get a splint or brace, or whatever, for my joints ... And nobody knows… And I don't know- I don't even know who to ask, do you know what I mean?"

[Mandy, Interview 016]

Participants' fears for the future also applied to decisions about having children. Due to the hereditary nature of JHS/EDS-HT, Bryn and Roger were worried about whether their children would inherit JHS/EDS from them:

> “Another worry is whether the baby’s got EDS? Because it's fifty-fifty percent, to pass it on.”
>
> [Bryn, Interview 011]

> “It's always that fear ... Of passing it on, and seeing someone else have to go through, what I've gone through? At the same time, I've got the experience to deal with it different. It's another one of them fears that yeah, does play on my mind.”
>
> [Roger, Interview 003]

Many of the participants in the present study had been diagnosed with JHS/EDS-HT much later in life. Some who had found out about their condition years after having families struggled with the guilt of having unknowingly passed JHS/EDS-HT on to their children:

> “So now my daughter is growing up, I feel- I didn't know I had EDS, if I’d have known, I wouldn't have inflicted this on anyone, and now I feel really guilty I passed on to her, but I didn't know.”
>
> [Lauren, Interview 006]

> “I think, when I first got diagnosed, I think my mum had felt quite a bit of guilt? Um, partly the ... Hereditary thing, thinking she's passed it on, sort of feeling, even though clearly she knew nothing about it, there's nothing she could have done.”
>
> [Mandy, Interview 016]

At times, the potential implications of JHS/EDS-HT on pregnancy, childbirth and heritability had been clumsily conveyed to participants by healthcare professionals and others:

> "… a GP- she looked it up online for me, and she did say, 'Ooh, you know, childbirth, you got a much higher chance of dying?', and I was like, 'What?'"
>
> [Wendy, Interview 015]

> "He was like, 'You should find out what gene it is, so you can prevent your children from having it ... And get-' I can't remember- 'preimplantation diagnosis.' And I'm like 'OH? WHAT? ... I'm here about my university work, not about my future possible children that I may, or may not have!'"
>
> [Frances, Interview 009]

Although some prior research has assumed JHS and some subtypes of EDS to be associated with severe pregnancy complications and premature delivery (Berglund *et al.*, 2000, Lumley *et al.*, 1994), recent research has indicated those with JHS and EDS-HT may not have any associated increased risk of preterm birth, stillbirth, or the need for a caesarean section (Sundelin *et al.*, 2017). Both JHS and EDS have been associated with a significantly increased risk of spontaneous abortion, the loss of a foetus before 20 weeks gestation (28% in JHS/EDS-HT vs 10-20% in the general population; (Larsen *et al.*, 2013)) therefore, in recent research, midwives and expectant mothers are advised to be alert during pregnancy for any potential sign of early delivery (Pezaro *et al.*, 2018).

5.14.3 A lack of psychological support

Many felt that psychological support to better cope with the stress and enduring psychosocial impact of JHS/EDS-HT on their lives was lacking. Disruption to behaviour, mood, and relationships with family, friends and colleagues can all occur

in the experience of a chronic pain condition such as JHS/EDS-HT, and the vast majority of participants described experiencing low mood, in addition to guilt, frustration and anxiety. Many wished for support when stressed, depressed or anxious; their fears about the future and worries about potential declines in their condition:

> "I think it's been a bit of a rollercoaster along the way, when I was first diagnosed there was that thing that's part relief, 'Okay, we know what it is, we've got a name for it, this is ... everything from the past, it all makes sense.' And then there's just this- I found, feeling of like, that it's genetic, that we can't fix this, what does this mean for the future? And almost like, starting going off, catastrophising, a little bit in my head? You know? 'I'm not going to be able to get married, or have kids', all the things that I thought I would."

[Mandy, Interview 016]

Mandy's catastrophizing reactions encompass a number of fears, including difficulties in keeping up with others and achieving life events such as having children or getting married. Again, fears and distress around thoughts of the future may be due to illness beliefs relating to a belief in a catastrophic decline in their abilities, and an inability to recover after a decline in health. Anna emphasised that while she could cope with her JHS/EDS-HT, she would appreciate support and help in her attempts to manage the condition on her own:

> "It's just ... I wanted to be there to manage when I'm having a bad day, and you know? My head hurts so bad from ... Trying to cope with everything. I wanted a way of making ... that stressy part of me to go away."

[Anna, Interview 014]

Neither Jackie nor Wendy felt that the psychological or emotional impact of JHS/EDS-HT was taken into account, despite the sometimes overwhelming number

of issues they had to cope with while living with JHS/EDS-HT, and its wide-reaching impact in their lives:

> "Nobody ... considers the psychological impact… I got diagnosed, and then was basically just told- even by [Consultant], 'Well, this is just going to get worse.' And then you get sent away! And no-one seems to think they've just given you a life-changing diagnosis."

[Jackie, Interview 017]

Jackie's doctor's admission that her JHS/EDS-HT was 'just going to get worse' may go some way to explaining the anxiety and fears of decline mentioned by several men and women in these results. While some participants had actively sought out emotional support during the course of their own self-management of JHS/EDS-HT, several participants were clear in describing the absence of psychological and emotional support, although they desired it, and how better emotional support would have the potential to improve their self-management of JHS/EDS-HT:

> "I liked the fact that you're looking at the mental side of it as well, and how it affects you emotionally, because I think that can get forgotten by doctors, sometimes…or at least it's not looked at as a whole package, necessarily."

[Wendy, Interview 015]

Interestingly, unlike recommendations for other chronic conditions, participants with JHS/EDS-HT did not mention the provision of patient education and support materials at diagnosis. In addition, it would seem from some participants' answers that there is a lack of awareness generally regarding how participants manage the cognitive and emotional impact of their condition.

5.15 Theme 5: Ways of coping

5.16 5.1 Psychosocial and cognitive appraisals:

5.16.1 Acceptance

Many cited acceptance of the life-long nature of their condition as having a beneficial impact, and acknowledged receiving a diagnosis as part of that. By recognising the need to pace and "*stay in sometimes because I just can't ... Do everything.*" [Georgina, Interview 008], participants were better able to manage the psychosocial impact of JHS/EDS-HT on their lives. Rhiannon had learned to accept that her body "*probably won't be able to do certain things*":

> "I'm a lot more ... accepting of it and I think the diagnosis has helped with that. I'm like, "Okay, I accept that this is a problem, and it's always going to be a problem", (background noise) And I just have to kind of- manage it, instead of-. Maybe in the past I would have thought, "Okay, how do I get rid of this?" or, "Why do I have this?" …So I think that, acceptance element is actually, probably, quite a big part of what has ... helped with it."

[Rhiannon, Interview 001]

Frances' acceptance of her JHS/EDS-HT had helped her to come to terms with the frustration and anger that she felt towards her body. By accepting that JHS/EDS-HT could not be fixed, she was able to move forward emotionally and become more understanding of the limitations that JHS/EDS-HT had on her life:

> "I think now, I'm like, 'Do you know what? I'm weird, and I'm bendy, and I'm always going to be that way, nothing is going to change how I am now.', you know? 'There's something wrong with me genetically, it's not something that can be fixed. […] I just have to accept it.'[…] so for a long while I was really angry with myself, aware of my body, that I couldn't just do what I wanted, couldn't just get better, couldn't just stop hurting, ... I think, just accepting it has just really helped, I think that's real problem for a lot of people, is just ...

> Accepting that it's there, and it's not going away? …And, once I did that, it's okay now."

[Frances, Interview 009]

Indeed, acceptance of a chronic condition, including its implications and limitations, has been found to be a common coping strategy employed among individuals with chronic conditions. Acceptance has been shown to be an important component in gaining an optimal sense of control (Walker *et al.*, 2004). Lauren and Jake emphasised the need to be optimistic and stay positive in the face of repeated setbacks:

> "If you have a really bad flareup, and you actually cannot do your exercises today ... just accept it and say, 'Okay, that's how I am at this point in time, but tomorrow is another day… I treat myself ... Maybe use hot packs, do a bit of meditation or something, listen to some nice music, or sit outside and look at the sunshine, or if it's freezing cold, sit inside and look out the window! (Laughs) But do something that makes you smile."

[Lauren, Interview 006]

> "My advice to anyone who has been diagnosed is, deal with it… Deal with it in the best way that you can. Try and stay positive, because it's the only thing that'll keep you going. This is not going to be easy, it's a shitty illness and no one understands."

[Jake, Interview 002]

Although JHS/EDS-HT had limited Frances' ability to '*keep up'* with her friends socially, she could still have a good time:

> "I think I'm just going to have to accept that I can't do everything that someone else my age could do, but you know what? I can still do stuff that I enjoy and have fun?"
>
> [Frances, Interview 009]

Most positively appraised their condition, feeling that JHS/EDS had made them more determined in the face of adversity and given them an inner strength to keep going that they had previously been unaware of:

> "I think there is quite a positive side as well? I think it's made me a better person, it's also made me more determined […] I feel like I've achieved something?[. .] At the end of it, even with all this going on and stuff, I haven't quit, and it's made me a better person, really?[. .]It's show me that I can be quite strong. That, ... Okay, this bit might be hard but we'll figure a way round this […] I can, kind of, dig deep, and keep going."
>
> [Mandy, Interview 016]

Many spoke of the need to harness their determination, to 'find a way' to complete the goals they had set their mind to:

> "So, I think while I'm still living, breathing, and talking, I'll just ... Get on with it! You know? And that's my attitude to it, really… You've just got to rather than think, 'I can't do it.' You've got to find- there's always a way, isn't there? You know? Nearly always a way."
>
> [Rachel, Interview 010]

> "I think it's just- just given me the slightly different attitude […] where there's a problem, looking for a solution, rather than just accepting 'no'. 'Is there a different way I can do this? Is there a different way around this problem?'"

[Jackie, Interview 016]

Participants had found relaxation and mindfulness helpful, particularly in relation to reducing anxiety and coping with pain:

> "But one of the things I do find though- Is that if I'm talking about pain, if I'm thinking about pain, I can actually feel my body tense… So then one has to start doing all the mindfulness thing, look at my breathing, and particularly the area that is quite tense is my shoulders, my lumbar area [. .] I've just got to be so focused about the fact that these areas are tensing up, saying to them, 'Slow down, deep breath, you're actually not in pain at the moment.'"

[Tabitha, Interview 012]

5.16.2 It Could Be Worse

All participants had taken time to find out more about their own condition, through websites, books, academic journals, and through support groups. However, as noted in the previous theme 'Fear of Future Decline', participants found that there was a lack of reliable information available to them. At support groups and online, participants could meet others who were more severely affected by JHS/EDS-HT:

> "[I'm] nowhere, as badly off as some of the girls are, you know? You just sort of look at them, twenty, thirty years younger than me in wheelchairs, walking with crutches, so far ... I don't need that."

[Tabitha, Interview 012]

Although frightening at times to see other, more severely affected others (as discussed in the *Fear of Future Decline* subtheme), by comparing themselves to others who had more severe JHS/EDS-HT or other life-limiting conditions, many participants felt that life '*could be worse'* and chose to see the positives in their own situation:

> "'I'm still fine, I'm still alive, there are worse things that I could have.', you know? ... My cousin's got MS? And my auntie had MS-… And, kind of look at them and think, 'They've got MS, it could be so much worse.' like, you know, 'I'm lucky, I'm all right, I'm not in pain most of the time.'"
>
> [Frances, Interview 009]

These downward social comparisons between participants and others with health conditions have been noted in the chronic illness literature as a means of boosting self-esteem and self-efficacy (Finlay and Elander, 2016). By seeing others suffering, participants are better able to reframe their own health status more positively in comparison, revealing new depths of coping and interpersonal learning (Finlay and Elander, 2016).

5.16.3 Social support

As friendship groups shifted, many participants made friends with, and gained social support from other people with JHS/EDS-HT or other chronic conditions. These 'similar friends' were perceived as more understanding and empathetic to what participants were going through. As Georgina put it, it was '*comforting to know you're not alone'* [Georgia, Interview 008]:

> "It's really nice to meet-just to know someone else who understands. And what's great is we can like, she can say- like, she's one of those people, again, who doesn't talk about their pain, so if I met her she knows she can? And I'm the same, that just feels really nice, that we have the understanding."
>
> [Emily, Interview 007]

> "I mean, the friends I do have now are the ones that are similar to me, not necessarily hypermobile but they've got mild disabilities. So they, at least, can

> relate. We can cancel each other for different reasons, I'll cancel on them because I'm tired, they'll cancel on me for various reasons […] So, I have ended up with more friends that are ... Disabled, in some other way, because they at least are accepting of the fact that I cancel seeing them"
>
> [Georgina, Interview 008]

Nigel found he had drifted away from the friends who had wanted 'energetic' or tiring nights out:

> "I suppose I veered away from all those friends, and stuck with the ones that are a little bit less ... How can I put it? ... exciting? So, it's now films, or a meal, rather than ... Five pints, and a, you know, nightclub."
>
> [Nigel, Interview 005]

The combination of social support and finding out more about JHS/EDS-HT gave participants the confidence and assertiveness to explain their condition to others when challenged:

> "So yeah, it doesn't particularly frustrate me, I see it as more of a chance to educate people about EDS, and other invisible illnesses. I'm really happy to talk about it. As I say, you start me off on it and I never shut up! So. (Laughs)"
>
> [Wendy, Interview 015]

> "Or ... I feel that, like, responsibility to educate people? And actually go, 'Yeah, there's a reason for this-'"
>
> [Mandy, Interview 016]

> "[After attending an inpatient Pain Management course] I've got the a-assertiveness to say, 'I'm going to sit down now,' or 'I need- I need to take a coffee break' you know, so that I can sit. Getting worse made it easier for me to explain to people in a very like, simplistic way…That I need to do things differently."
>
> [Emily, interview 007]

5.17 Physical and Behavioural

5.17.1 Hobbies and projects

Most participants had adapted their activities to better manage the overall impact of JHS/EDS-HT. Participants cited accessible hobbies and projects as a way to keep themselves '*sane'*. Nigel had always really enjoyed DIY and got great enjoyment from hands-on building projects, but the impact of such activities left him *'completely ruined'* for weeks after. Later, he found a good substitute to give him the same level of happiness and satisfaction, which he felt occupied his mind from '*dwelling on things'*:

> "…It's going to sound really silly ... It's Lego… because I can do that sitting down, I haven't got to, you know ... expand too much energy by doing it, and I get almost the same satisfaction out of doing that, which I found, it's helped my-my self-esteem, and my mental side of it, more than anything."
>
> [Nigel, Interview 005]

Mandy found that by adapting her activities to better work with her own body, she could still keep swimming and dancing, but '*slightly differently'*:

> "I used to be really active, dancing, swimming, running, that kind of stuff. So that's had to be adapted ... quite a lot. Um, but I've learnt a different way of swimming… just using one arm, not the one that dislocates all the time. I've kept

> the swimming up now, I've got that way of doing it, I'm gradually building up how many lengths can do, and that kind of thing, so it's getting back to something that I used to really enjoy, just doing it slightly differently."

[Mandy, Interview 016]

Claire had changed her motorbike to a model that caused less strain on her hips:

> "So, I did a trade-in… they sorted me out with a good bike ... Throughout my life, I've created my own workarounds for doing things… So, it's kind of, just building on that again."

[Claire, Interview 013]

Rachel found the double benefit of fewer dislocations and improved wellbeing when she walked with her dogs:

> "It's that feeling of well-being, you know? I feel happier when I exercise, this is why I love walking my dogs, I go for a hill walk for an hour or two ... You come back, and you feel wonderful, and I like that feeling, and it is that slightly euphoric feeling you get when you exercise, and I like that, and I feel like I need to do that, so that is a really big thing for me, keep moving, keep moving and exercise yeah."

[Rachel, Interview 010]

In addition to adaptations, almost all recommended supporting joints with splints and braces and had found that pacing their activities with rest worked well. Participants learned which exercises worked best for them through a system of trial and error:

> "I kind of learned, over time, what- which moves I can do and which moves I can't do and I just- I just try to be sensible with that."
>
> [Rhiannon, Interview 001]

> "I did try swimming, and swimming itself helped me to build muscle and stuff, I found it so exhausting though, it just didn't help […] Pilates really, really helps, so ... Particularly with dislocations, I suffered dislocations a lot less when doing that, because it built muscles in the right places."
>
> [Wendy, Interview 015]

5.17.2 Positive interactions with healthcare professionals

Although participants reported that some exercises made their pain worse (see Limitations to current treatment subtheme under Theme 2), others had reported very positive experiences of physiotherapy. These treatment plans were with physiotherapists who had specialist JHS/EDS-HT knowledge, or clinicians who had taken the time to research JHS/EDS-HT themselves:

> "The physios there are hyper- their area of interest is hypermobility…So they- they know their stuff![. .] But I would say that's quite rare."
>
> [Rhiannon, Interview 001]

Physiotherapists also provided some emotional support and encouraged regular exercise.

> "But my physio I have, she knows my condition quite well […] At times I used to be more- I still am- frightened of what the future holds, erm, how the Ehlers-Danlos is going to get worse, or how it might affect me? […] she's shown me techniques … if I feel my shoulders dislocating, how to put them straight back

> before it comes out and things like that. So I'm not as, frightened in some respects? Erm, there's a bit more light at the end of the tunnel."
>
> [Roger, Interview 003]

Emily's physiotherapist encouraged her to adapt her activities:

> "And something one of the physio's said to me, which was, 'You can do anything that you want to', and like for me that really like ... Hit a bell, like, 'Can I?', And she said, 'You can' . And that's- I always think that I can do anything, I just have to find my way of doing it."
>
> [Emily, Interview 007]

While healthcare professionals may not always recognise the condition, participants were pleased when their GP was willing to learn:

> "The GP I originally went to didn't know much about it at all, really. But she kind of- acknowledged that? So I don't- I don't think that was necessarily a problem?.. And she did kind of- go away and, look it up and talk to colleagues about it…I was lucky though, with her, I imagine other healthcare professionals if they didn't know as much about it maybe would have been a bit more dismissive?"
>
> [Rhiannon, Interview 001]

As Jake put it, "*it's more… how they respond to NOT knowing, than what they know.*" [Interview 002]. Several participants acknowledged that GPs could not be expected to know everything about obscure genetic disorders. However, others felt that greater training and awareness of JHS/EDS-HT among HCPs could improve outcomes for patients:

> "I personally think if a GP does have a patient with a certain condition they should go on training, they have conferences every year? That would be helpful[. .] and they need to do that, the patient does have a rare condition."

[Bryn, Interview 011]

> "So I think, having the understanding of the professional would be ... Really good, for others. Um, I don't feel that GPs are informed enough, or clued up enough."

[Anna, Interview 014]

Often, it was not that a treatment had worked, but that healthcare professionals had taken the time to listen non-judgmentally to patients "*rather than just ... Pacifying you, and sending you away*." [Mandy, Interview 016]. By acknowledging the multidisciplinary impact of JHS/EDS-HT and providing useful guidance such as leaflets, healthcare professionals could prevent participants from feeling that their condition was not recognised:

> "The other thing [that] is very important, is just being believed."

[Tabitha, Interview 012]

5.18 Reflexivity: Acknowledging potential influences

One potential influence on these findings is the participants recruited. Although an excellent source of patients with JHS/EDS-HT, recruiting from EDS-UK and the local NHS Trust required participants to self-report their symptoms of JHS/EDS-HT. Although requirements such as the Hakim and Grahame (2003) Five-Point questionnaire were included to prevent participants who were not hypermobile from being recruited, some participants may have been able to submit responses

without a confirmed diagnosis of JHS/EDS-HT. Given the highly detailed reports and responses, it is unlikely that any of the 17 participants finally chosen for this study did not have JHS/EDS-HT, but it was an important factor to consider. In addition, those recruited from support groups may be more actively involved in their condition and have greater JHS/EDS-HT-related knowledge than those who are not. However, some were only members of the group's social media platforms and had not paid for membership. In addition, a significant minority of participants had not attended support group events, or had attended but decided that real-world involvement in the JHS/EDS-HT support group community was not for them, instead preferring to either contact others online, or rely on their own sources of information.

Lastly, another consideration is the results of the systematic review and thematic synthesis conducted by the researcher and presented in an earlier chapter of this thesis. The review sought to provide a comprehensive overview and thematic synthesis of all JHS/EDS related literature relating to the lived experience of the condition and published within the previous 27 years. As the results of the review were then used to shape the questions posed to participants, and gave a greater overview of what had, and had not been covered by previous research, it is possible that these results may have influenced the Study 2 findings.

While it is never completely possible to remove a researcher from any external influence, steps were taken to ensure that these findings did not have bearing on what participants had shared. Understandably, similarities between what participants in this study shared, and what JHS/EDS-HT research had previously covered was inevitable, however the researcher was careful to remain open to all possibilities during the transcribing, coding and analysis phases. In the conduct of any research study, the researcher must have an overview of the type of data they are required to collect and the population under study; this knowledge is vital to be able to collect all data in a standardised manner (Rwegoshora, 2006). In order to reduce the subjectivity of the research findings, any potential bias can be negated by gaining secondary advice and independent input from a multidisciplinary research team (Rwegoshora, 2006). As previously mentioned in Chapter 2, the research supervisory team, as experienced researchers, objectively checked the coding

interpretations in an effort to safeguard from any potential researcher bias or influence from previous findings (Pope and Mays, 1999, Tinker and Armstrong, 2008).

5.19 Discussion

This study provides a novel understanding of how psychosocial factors, such as the support of family, social networks and attitudes of healthcare professionals are perceived to play significant roles in shaping men's and women's experiences of JHS/EDS-HT.

Invalidation can be a common problem with rheumatic diseases (Kool *et al.*, 2009), and involves a lack of understanding or negative social responses from others, such as disbelief, rejection, stigmatisation and suspicion that the problem may be psychological (Kool *et al.*, 2009). As with other examples within the literature, participants in this study experienced long waits for diagnosis, allegations of hypochondria, and a lack of understanding and knowledge of the condition from healthcare professionals (Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016, De Baets *et al.*, 2017, Palmer *et al.*, 2016a).

Pain and fatigue, the main symptoms in JHS/EDS-HT, are mostly non-observable by others; therefore participants' symptoms and associated burden of the condition were often cited as being poorly understood. Participants hid their symptoms in an attempt to appear 'normal' and avoid confrontation. Shame, guilt and stigma can have negative psychosocial consequences, lowering self-esteem and in some cases leading to depression (Van Brakel, 2006). Interventions to address issues around self-esteem in chronic pain populations have targeted social functioning, including anger management, depression and self-esteem (Barlow *et al.*, 2002, Dwarswaard *et al.*, 2016). Therefore, future psychosocial interventions and support to address feelings of stigma and improve participant's self-esteem would be valuable.

Others recounted significant pain from reduced effectiveness of local anaesthetics, thought to be due to the underlying collagen defect in JHS/EDS-HT (Wiesmann *et al.*, 2014). These experiences could lead to a fear of treatment, which

may prevent those with JHS/EDS-HT from seeking appropriate medical care (Berglund *et al.*, 2000). When finally diagnosed, participants reported feeling great relief at understanding their condition, similar to other JHS/EDS-HT research (Palmer *et al.*, 2016a, Terry *et al.*, 2015). Some progress is already being made towards improving awareness of JHS/EDS-HT amongst general practitioners through a newly published EDS GP Toolkit, in partnership with the Royal College of General Practitioners (RCGP) and Ehlers-Danlos Support UK (EDS-UK) (Reinhold *et al.*, 2018). However, there is still an overall lack of training and awareness of JHS/EDS-HT among GPs and healthcare professionals, and the guidance does not cater for the psychosocial impact of the condition.

In addition to difficulties with local anaesthetics, recent important research by Rombaut et al (Rombaut *et al.*, 2015) and Scheper and colleagues (Scheper *et al.*, 2017) also indicated significant hypersensitivity to pain in patients with JHS/EDS-HT, compared to the general population. Generalised hyperalgesia, defined as an abnormally increased sensitivity to pain, could leave this population more prone to chronic pain and fatigue (Rombaut *et al.*, 2015, Voermans *et al.*, 2010). Therefore, the tailoring of multidisciplinary pain management interventions, including cognitive behavioural therapy and physiotherapy would be an important consideration, in order to reduce overall disability and improve patient quality of life (Rombaut *et al.*, 2015).

Participants with JHS/EDS-HT experienced numerous restrictions to their lives as a result of a range of symptoms, including pain, fatigue and the unpredictability of their condition. Additional multifactorial symptoms, in combination with environmental factors such as social stigma or isolation may contribute to psychological distress and disability in this population (Scheper *et al.*, 2016).

Issues around the effects of pelvic organ prolapse in JHS/EDS-HT echo a recent questionnaire survey which found more severe sexual dysfunction and a greater negative impact on quality of life in women with JHS compared to the general population (Mastoroudes *et al.*, 2013). Difficulties with sexual relationships due to vaginal or bladder prolapse in women, or erectile dysfunction in men are an under-researched finding; participants feared a negative impact on their relationship, and were unsure of what could be done medically to solve their

problems. Erectile dysfunction can also be a symptom of autonomic dysfunction (common in POTS), which has been linked to sexual dysfunction in Parkinson's disease (Meco *et al.*, 2008). However, there has been little assessment of this issue within the JHS/EDS-HT literature (De Wandele *et al.*, 2014).

A scarcity of information and dependable psychological support for JHS/EDS-HT led some to be very fearful of future declines in their ability. Information on the internet was also highlighted by participants, and are a new consideration in this area. Several participants described these fears as leading to catastrophising and feelings of panic when faced with new symptoms, in case this signified their own decline (Beck, 1985). In addition, when people make social comparisons to others in the same chronic illness group there is a risk that other support group members' decline could be interpreted as a representation of their own future, resulting in negative feelings (Buunk *et al.*, 1990, Heaton, 2015, Tennen and Affleck, 2000, Festinger, 1954). Due to the hereditary nature of the condition, this is particularly relevant to children whose parents also have JHS/EDS-HT. Psychosocial factors such as fear-avoidance behaviours, activity limitation, catastrophising and fear of movement may substantially contribute to increased levels of disability in this patient group, as has been seen in other chronic pain populations (Gatchel *et al.*, 2018, Turk and Okifuji, 2002). In this case, maladaptive beliefs relating to JHS/EDS-HT (such as the belief of a sudden decline) appeared to lead to heightened emotional reactivity, leading to catastrophising, anxiety and feelings of panic (Turk and Okifuji, 2002).

In order to counteract this effect, it may be beneficial for support group members to be provided with opportunities for positive social comparison, as interaction with other patients has been shown to help reduce fear relating to symptoms (Grahn and Danielson, 1996). Modeled behaviour involves providing example behaviours for people to aspire to or imitate (Michie *et al.*, 2011). In line with Bandura's Self-Efficacy Theory, self-efficacy relates to an individual's expectations and beliefs about their ability to perform specific actions effectively (Krouse, 2001). Video modeling, or the demonstration of desired behaviours through visual media, has been used successfully in patient education and to facilitate learning of new skills (Krouse, 2001), including in prostate (Partin *et al.*, 2004), breast

(Janda *et al.*, 2002) and colorectal (Zapka *et al.*, 2004) cancer screening, and adherence to self-care behaviours for participants with heart failure (Albert *et al.*, 2007). By using models to promote exemplary behaviours, video modeling can serve as a useful way to promote self-efficacy in others (Bandura, 1997). For instance, examples of self-help ideas and positive coping strategies could be promoted by those with JHS/EDS-HT using video clips, for people experiencing a flare in symptoms.

These results also demonstrated the physical and psychosocial impact of JHS/EDS-HT in terms of adjustment and adaptation to the condition, extending knowledge regarding coping strategies employed by those with JHS/EDS-HT. Initially, diagnosis was met with relief, but later reactions indicated that participants had to face changes in how they saw themselves, and how others perceived them. Chronic illness and disability can bring about great changes in a person's identity (Cook *et al.*, 2017). Many cited acceptance of JHS/EDS-HT as positively influencing their ability to cope. Acceptance in this case can be defined as refocusing attention on aspects of the condition that they can control, rather than struggling to control pain (Hayes *et al.*, 1999). These findings are similar to other studies, which found that acceptance promoted adjustment to chronic disease (Kostova *et al.*, 2014, Costa *et al.*, 2014, Kirkpatrick Pinson *et al.*, 2009). In addition, rheumatic diseases research has indicated that acceptance of a pain condition, in addition to high self-efficacy, can have a buffering effect against invalidation by others, such as healthcare professionals, friends or family (Cameron *et al.*, 2018). Participants who identified a need for greater psychological support indicated that this should be available as soon as possible following diagnosis in order to better support this transition.

Building social networks and social support were also cited as useful coping strategies by participants, including joining support groups and making friends with others who had JHS/EDS-HT. Online and face-to-face support communities play an important role for those with chronic diseases in conveying information, gaining emotional support and comparing experiences (Weis, 2003, Coursaris and Liu, 2009). By gaining knowledge about their condition, participants were able to foster a sense of control, and lessen the feelings of '*unknown'* and fear that can be present in unpredictable conditions (Thorne *et al.*, 2002, Kirkpatrick Pinson *et al.*, 2009).

In line with prior research (Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015) participants described how becoming dependent on others for help with activities could result in feelings of guilt and shame. This highlights a need for greater support for participants with JHS/EDS-HT in order to maximise independence in everyday activities, particularly in relation to personal care, washing and dressing. This is a key indication that rehabilitation and support for people with JHS/EDS-HT needs a greater focus on maximising independence in activities of daily living.

Many participants' actively adapted hobbies and sports to better achieve their ambitions. Healthcare professionals such as physiotherapists with knowledge of JHS/EDS-HT were cited as helping them to achieve their goals. By giving patients an indication that things could improve, physiotherapists gave patients hope. Encouraging patients to adjust to daily life may lead to a sense of control and stimulate active coping strategies. A recent qualitative study of physiotherapy for JHS recommended a holistic approach to management, rather than treating single joints in isolation (Palmer *et al.*, 2016b). Specialist physiotherapists with knowledge of JHS were cited as being very helpful. However, building on the dearth of specialist JHS/EDS-HT support highlighted in Chapter 3, specialist physiotherapy for JHS/EDS-HT is limited in the UK, and there is little consensus regarding optimal exercise (Palmer *et al.*, 2014). Further exploration of patient and healthcare professionals' ideas about optimising supportive interventions for JHS/EDS-HT would be valuable.

5.19.1 Strengths and Limitations

This is the largest study of participants' lived experiences of JHS/EDS-HT, compared to previous semi-structured interview studies (n=10, (De Baets *et al.*, 2017); n=11 (Schmidt *et al.*, 2015, Berglund *et al.*, 2000)). In addition, this study had a proportionally higher representation of participants of mixed ethnicity. While hypermobility is known to affect Black and Asian populations to a greater extent (Connelly, 2015), very few ethnically diverse participants have been involved in JHS

and EDS research compared to participants of White ethnicity. While this study purposively sampled to gain a broader representation, further work is still required to assess whether any new themes would be identified with greater representation of black and minority ethnic populations, whose views in JHS/EDS research have yet to be explored in great depth. While men were involved in this study, their experiences of JHS/EDS-HT compared to women have yet to be fully studied.

Furthermore, while the position of the first author (SB) as both a patient and a researcher could be considered a strength, I was also aware of the possibility of bias as a result of this dual position. While bias cannot be eliminated entirely, it can be mitigated (Malterud, 2001). In order to counteract this, the first author (SB) kept a reflective practice research diary exploring my feelings and reflections after each interview. A random selection of recordings was checked against transcripts by the research team (NW, TM, SP), thereby allowing those not directly involved in data collection to audit the results, reducing potential bias and ensuring accuracy (Malterud, 2001). Peer debriefing was used to safeguard externality, where the research team (NW, TM, SP) reviewed the findings and themes identified in the results. This allowed me the chance to think more critically about the research, and to discuss and explore judgements made about the data.

5.19.2 Implications for clinical practice

These findings have built upon previous findings in this area, including sexual dysfunction (Palmer *et al.*, 2017), and requirements for improved awareness among healthcare professionals (Berglund *et al.*, 2010, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016a). New topics have also been established, such as a need for greater independence in activities, fear regarding symptoms and decline, and the risk associated with social comparisons to others with JHS/EDS-HT. The importance of social support, patient groups and communities was highlighted, as was the need for future interventions to improve feelings of stigma and boost self-esteem. It would be helpful to map what is now known about the psychosocial impact of JHS/EDS-HT to behaviour change theories, such as the Theoretical Domains Framework or COM-B (Michie *et al.*, 2005b, Michie *et al.*, 2011). This could help to

develop focused behaviour change interventions based around factors identified by patients as promoting or hindering their ability to cope with JHS/EDS-HT.

5.20 Conclusion

The objectives of this study were to identify the psychosocial impact of JHS/EDS-HT by examining participants' lived experiences, and to identify characteristics of effective coping with JHS/EDS-HT. The themes identified by participants are similar to those experienced by patients with other chronic pain conditions with similar symptomology, such as systemic lupus erythematous (SLE). For example, patients with Lupus have also reported a lack of understanding from their healthcare professionals, which made them reluctant to contact their doctors due to a perceived lack of empathy (Squance *et al.*, 2014). This exploratory chapter comprehensively detailed adult men and women's experiences of JHS/EDS-HT and provided a novel understanding of how psychosocial factors, such as the support of family, social networks and attitudes of healthcare professionals all play significant roles in shaping men's and women's experiences of JHS/EDS-HT. Several coping approaches were identified by participants, including building social networks, finding out more about JHS/EDS-HT, adapting their activities to better manage the impact of the condition and a need to educate healthcare professionals involved in their care. The findings of this study, in addition to those of the next phase will be discussed in further detail in the final discussion chapter of this thesis.

6 Chapter 6: Determining recommendations for a self-management intervention to manage JHS and EDS-HT using behaviour change theory: A mapping exercise

6.1 Introduction

This chapter provides an overview of how the results from the Study 1 systematic review in Chapter 4 and the Study 2 qualitative interview results in Chapter 5 were mapped to two behaviour change theories: the Theoretical Domains Framework, and the COM-B. This mapping allowed for triangulation of the findings in each section of the PhD, and from this mapping exercise a number of potential behaviour change interventions were actively identified, based on barriers that participants with JHS/EDS-HT identified for the effective self-management of their condition.

This chapter outlines Study 3; the mapping of results, and the use of a focus group of experienced researchers and a Patient Research Partner to refine the process. Lastly, the resulting potential behaviour change interventions identified during the mapping and refinement processes were presented to two modified Nominal Group Technique (NGT) focus groups with patients who have JHS/EDS-HT. In the two focus groups, participants with self-reported JHS/EDS-HT (n=9, all women) were encouraged to vote for their preferred intervention options and to discuss the feasibility, acceptability and any potential barriers or facilitators to the implementation of their top two intervention options. These results will be considered and discussed at the end of this chapter.

6.2 Background

Research has indicated that the chronic joint pain associated with JHS/EDS-HT can have a significant emotional and psychosocial impact (Smith *et al.*, 2014b). Recent

systematic reviews have found that those with JHS suffered significantly greater psychological distress compared to those without the condition, namely anxiety (Sanches *et al.*, 2012, Smith *et al.*, 2014b), depression and panic disorders (Smith *et al.*, 2014b). The multifactorial impact of JHS and EDS-HT can lead to poor health-related quality of life and restricted physical and psychological functioning (Berglund and Nordstrom, 2001, Maeland *et al.*, 2011). A lack of professional awareness of the syndromes can cause considerable delay in diagnosis, and the otherwise normal outward appearance of patients can lead healthcare professionals to question the legitimacy of patients' pain and symptoms (Berglund *et al.*, 2010). An earlier stage of this research further built on these findings with qualitative interviews (n=17), which gave an in-depth understanding of how psychosocial factors such as condition-specific knowledge, the support of family, social networks and attitudes of healthcare professionals all play significant roles in shaping men's and women's experiences of JHS/EDS-HT.

There is currently little UK guidance for managing and supporting patients with JHS/EDS-HT (Palmer *et al.*, 2016b). Patients have indicated that healthcare professionals may struggle to understand or manage their condition (Berglund *et al.*, 2000, Lumley *et al.*, 1994). An anecdotal risk of physical deconditioning has also been recognised, which may lead to a worsening of symptoms and pain over time (Hakim *et al.*, 2017). While physiotherapy is a mainstay of treatment, evidence for its effectiveness is limited (Palmer *et al.*, 2014), and physiotherapists can be at a loss as to how to treat patients with JHS (Palmer *et al.*, 2016a). Participants in an earlier stage of our research expressed that they would like to receive greater support and guidance in managing their condition, particularly after diagnosis, but that NHS provision for this was lacking.

Use of the Theoretical Domains Framework (TDF) in published research

The TDF framework has been used to explain the challenges inherent when implementing a behaviour change intervention. These can include factors such as the barriers and enablers to hand hygiene behaviour (Dyson, 2015); barriers to implementing guidelines in schizophrenia (Michie *et al.*, 2007) and the barriers and facilitators encountered by midwives when encouraging pregnant women to stop

smoking (Beenstock *et al.*, 2012). The TDF has also been used to identify enablers and barriers to the implementation of evidence-based clinical guidelines for low back pain (Mckenzie *et al.*, 2010) and in combination with the COM-B to understand recruitment to NHS pharmacy smoking cessation programmes (Sohanpal *et al.*, 2016).

It has also been used to guide the development of interventions, including management of mild traumatic brain injury in the emergency department (Tavender *et al.*, 2015), dentist's promotion of smoking cessation counselling (Amemori *et al.*, 2011), blood transfusion prescribing behaviours (Francis *et al.*, 2009) and in the development of an intervention to improve physiotherapists' management of falls risk after discharge from hospital (Thomas and Mackintosh, 2014).

More relevantly, the TDF has been used to develop intervention strategies. Fleming and colleagues (2014) used both the TDF, COM-B and Behaviour Change Theory (BCT) taxonomy (a precursor to the COM-B) to examine healthcare professionals' views of antibiotic prescribing behaviours in long-term care facilities (LTCFs). Interviews with 37 healthcare professionals who worked in LTCFs were mapped to the TDF, BCW and TDF in order to recommend intervention strategies. The results found that antibiotic prescribing was influenced by a variety of social and contextual factors, including variable knowledge in antibiotic guidelines, a lack of training for pharmacists, and time constraints. Recommendations included educational information about antibiotic prescribing guidelines, persuasion of importance of not over-prescribing antibiotics, practice in referring to the guidelines in daily care, and the option for a financial incentive to staff if antibiotic prescribing targets were met (Fleming *et al.*, 2014).

Similarly, the TDF was used in combination with Behaviour Change Techniques (BCTs) to define the content and delivery of an intervention to improve treatment adherence in Bronchiectasis (Mccullough *et al.*, 2015). Semi-structured interview data from patients with bronchiectasis about barriers and motivators to adherence to treatment, along with focus groups and interviews with healthcare professionals was coded to the TDF to identify relevant domains. These mapping results were presented to three expert panels (two with patients and one with healthcare professionals and academics) in order to determine who the intervention

should target, who should deliver it, the format and setting of delivery, and how efficacy should be measured. Results indicated 8 relevant TDF domains identified by both healthcare professionals and patients, and 12 behaviour change theories (BCTs). These included patients' lack of '*knowledge'* (TDF domain) regarding the need for inhaled antibiotics, knowledge of disease progression, and '*social influences'*, such as the support of healthcare professionals and other people with bronchiectasis in managing their own condition. However, some feared becoming a burden on their family members. Patients suggested a need for training on treatment skills, information on disease progression, reasons for treatments and expected consequences of non-adherence in order to encourage patients to adhere to their bronchiectasis treatments (Mccullough *et al.*, 2015).

As discussed at length in Chapter 3, the TDF was therefore deemed appropriate in the current context to understand the components of behaviour that may be addressed to allow people with JHS/EDS-HT to better manage their condition.

6.2.1 Aims and objectives

6.2.1.1 Aim:

To determine recommendations for the components of a behaviour change intervention for people with JHS or EDS-HT.

6.2.1.2 Objectives:

1. Using the COM-B model and Theoretical Domains Framework (TDF) to identify what would be required to change for patients to better manage JHS/EDS-HT (a behavioural analysis).
2. To identify which behaviours identified by the COM-B mapping exercise could potentially be modified, using the COM-B taxonomy (Michie *et al.*, 2011).

3. To identify which factors should be prioritised and preferences for intervention content, from the perspectives of people with JHS/EDS-HT, using a Nominal Group Technique.

6.3 Ethical approval

Approval for the study was obtained from the University of the West of England Faculty Research Degrees Committee (UWE REC REF No: HAS.18.03.128, 27th April 2018, Appendix L).

6.4 Methods:

6.4.1 Research Design

The BCW builds upon recommendations by the Medical Research Council (MRC) that a coherent theoretical model should be used when developing health promotion methods and complex behaviour-change interventions (Craig *et al.*, 2008). However, many published interventions lack a clear theoretical underpinning, or theories were poorly applied and not linked to effectiveness (Prestwich *et al.*, 2014). In order to develop a robust intervention, the BCW, comprised of the TDF and COM-B, has been used to devise a self-management behaviour change intervention. The TDF and COM-B are also recommended in National Institute for Health and Care Excellence (NICE) policy guidelines for behaviour change interventions that meet individual needs (National Institute for Health and Care Excellence, 2014a). The stages in this section of the thesis are outlined in Figure 6A below. The BCW recommends three key stages in developing an intervention, which correspond to the three stages of intervention development recommended by the Medical Research Council (MRC, (Craig *et al.*, 2008):

6.4.1.1 Stage 1: Understanding the behaviour

- Conduct a systematic review and thematic synthesis of published qualitative data, in order to better understand adults' lived experiences of JHS and EDS (Study 1, Chapter 4).
- Conduct a series of interviews with UK adults who have JHS/EDS-HT, in order to understand the psychosocial impact of their condition, and the methods that they employ to cope with JHS/EDS-HT (Study 2, Chapter 5).
- Map the results of these two chapters onto the TDF, COM-B and BCW, in order to accomplish a behavioural analysis (Study 3, Chapter 6).

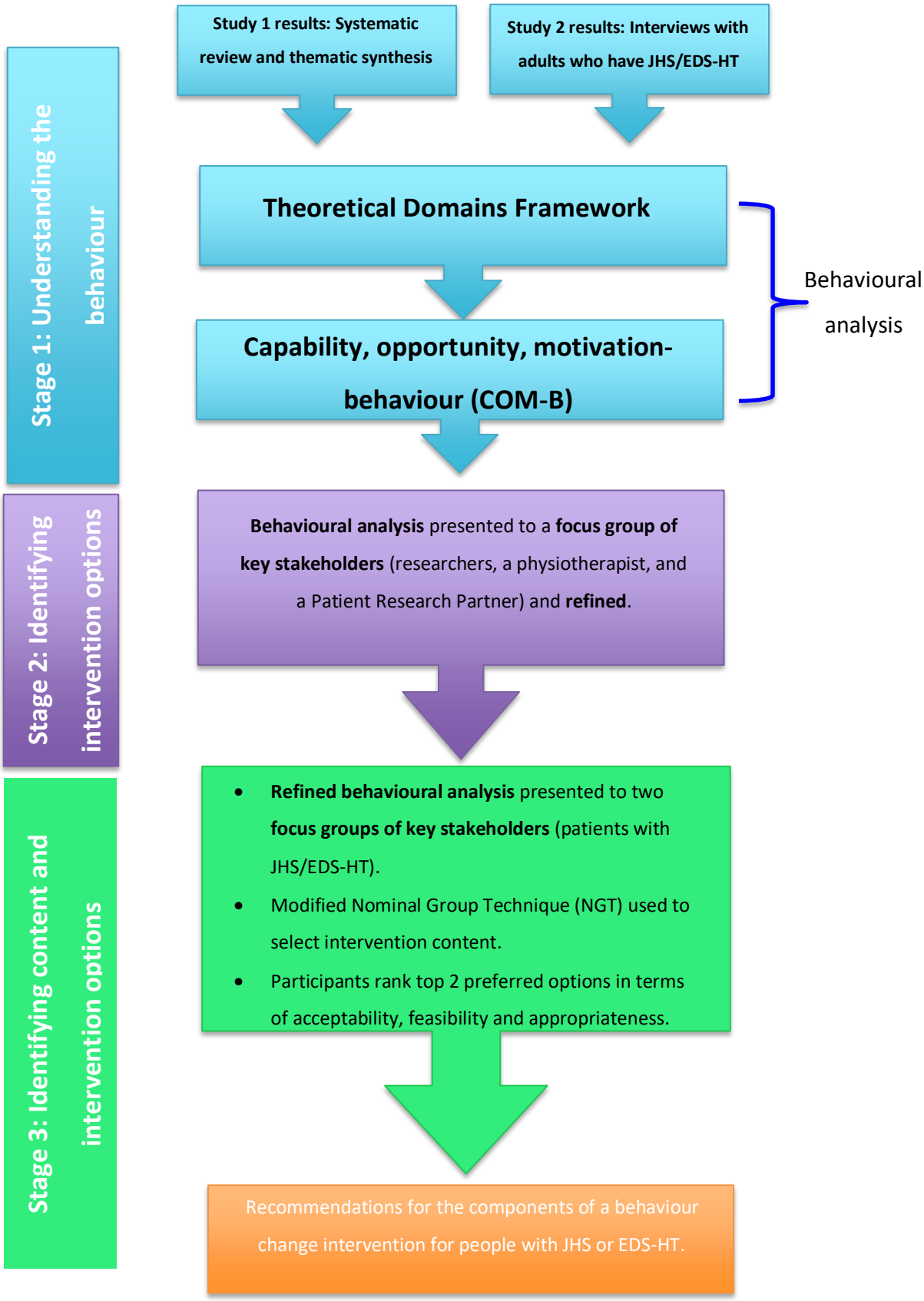
6.4.1.2 Stage 2: Identifying intervention options

- Using the results from Stage 1, identify and select intervention functions for the self-management of JHS/EDS-HT, using a focus group of key stakeholders, involving researchers with quantitative and behavioural change expertise, a physiotherapist and a Patient Research Partner.

6.4.1.3 Stage 3: Identifying content and intervention options

1. Conduct two focus groups with people who have JHS/EDS-HT and use group consensus methods (modified Nominal Group Technique) to identify and select preferred content.
2. To discuss participants' top two preferred intervention options in terms of appropriateness, acceptability, feasibility, perceived barriers and potential solutions.

Figure 6A: Flow diagram showing the different stages of the behaviour change intervention design process.



6.5 Stage 1- Understanding the behaviour

6.5.1 Mapping existing primary data to COM-B and TDF: What do participants need to do differently to improve self-management of JHS/EDS-HT?

The first step in the process involves understanding the problem, in this instance the behaviours are those employed by men and women with JHS/EDS-HT in order to self-manage their condition.

When collecting information to identify what needs to change, Michie and colleagues (2015) argue that data needs to be collected from as many relevant sources as possible, as the most accurate representation will be gained by using input from multiple perspectives (Michie *et al.*, 2015). By triangulating data from multiple published sources, all using first-hand qualitative interactions with participants who have JHS, EDS (in the case of the systematic literature review in Study 1) or EDS-HT, we can gain a greater insight into the potential barriers to self-managing JHS/EDS-HT. Therefore, in order to gain as broad a range of the data as possible, the results of Study 1, a systematic review of all qualitative JHS/EDS research relating to patients lived experience (Bennett *et al.*, 2019a) and data from Study 2, qualitative interviews exploring the psychosocial impact of JHS/EDS-HT with UK participants with JHS/EDS-HT (Bennett *et al.*, 2019b) were chosen for the mapping process.

The systematic review data from Study 1 includes the results sections of nine studies examining patients' experiences (Berglund *et al.*, 2010); lived experiences (Terry *et al.*, 2015); perceptions of daily life with EDS (Berglund *et al.*, 2000); lived experiences concerning diagnosis, daily life with EDS-HT and becoming a mother (De Baets *et al.*, 2017); decisions about activity (Schmidt *et al.*, 2015); views of physiotherapy (Palmer *et al.*, 2016b); and experiences of physiotherapy (Bovet *et al.*, 2016, Simmonds *et al.*, 2017, Simmonds *et al.*, 2016). The qualitative interview data from Study 2 explored and expanded upon these findings with 17 men and women from across the UK, identifying the psychosocial, cognitive and behavioural impact of

JHS/EDS-HT by examining participants' lived experiences of the condition (Bennett *et al.*, 2019b).

The results of the Study 1 systematic review indicated that participants with JHS and EDS experienced a lack of understanding from healthcare professionals, before and after being diagnosed. The fluctuating nature of JHS and EDS with cycles of injuries led to participants living restricted lives to avoid injury and aggravating factors. The hidden nature of JHS and EDS gave participants the opportunity to appear 'normal', but they faced criticism from those who didn't understand their condition, resulting in negative thoughts and feelings about themselves. Participants' dependence on others for help and their struggles to "keep up" with others resulted in feelings of guilt and shame. The theme 'Gaining control' involved negotiating physiotherapy, guiding their own affected children and learning to live with their condition (Bennett *et al.*, 2019a).

Qualitative interviews in Study 2 indicated that participants with JHS/EDS-HT experienced numerous restrictions to their lives as a result of their symptoms, and of the unpredictable nature of their condition. Although social groups could be difficult to navigate, participants tended to be friends with -and compare themselves to- others with the same or similar conditions. Participants also experienced very long waits for diagnosis, and a lack of understanding and knowledge of the condition from healthcare professionals. A scarcity of reliable information regarding JHS/EDS-HT and dependable support for their condition led some to be very fearful of future declines in their ability, and some panicked when faced with new symptoms. In terms of coping, participants relied upon self-sourced information, social comparisons and social support to better manage the psychosocial impact of the condition. To manage the physical and behavioural aspects, many actively adapted their hobbies and sports to suit them, citing knowledgeable healthcare professionals as helping them to achieve their goals (Bennett *et al.*, 2019b).

Mapping to the TDF and COM-B was achieved using Microsoft Word, with matrix tables used to map the data according to the themes identified by the prior thematic analysis and thematic synthesis. If any area of the mapping process was unclear, this was discussed with the supervisory team to reach consensus. The data was independently mapped by the PhD student (SB), to the TDF domains, and then

the COM-B, and is outlined in Table 6.1 below. In order to categorise what would need to change in order for participants to effectively self-manage JHS/EDS-HT. All themes and subthemes identified for the thematic synthesis and thematic analysis were mapped, first to the TDF, then to the COM-B domains. Mapping in this case refers to the matching process between qualitative barriers identified by participants to the relevant subsections of the TDF and COM-B and then to intervention functions. The potential intervention functions, with their associated mapping categories were presented in a final table, with themes represented under each of the six COM-B subdivisions (See Appendix M). All TDF domains were coded as part of the analysis. The most frequently coded TDF domains were *Knowledge, Emotions, Social influences, Social/professional role and identity, Skills, Beliefs about capabilities, Beliefs about consequences*. While not coded as frequently, codes were also identified for: *Environmental context and resources, reinforcement, goals, intentions, behavioural regulation,* and optimism.

Table 6.1: Mapping barriers identified in Study 1 and 2 to the COM-B and TDF.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Lack of awareness of JHS/EDS-HT within clinical settings or how to treat appropriately. Examples: ○ GP's were not always aware of JHS/EDS-HT and how to assess. ○ Lack of knowledge of the syndrome in primary care. ○ Long journey to diagnosis. ○ Accidental injury of patients in primary care. ○ Lack of knowledge of potential local anaesthetic failure.	○ Knowledge.	○ Psychological capability.	○ Education strategies ○ Training. ○ Enablement.	1. Informative JHS/EDS-HT leaflets and guidance. 2. Increase healthcare professional (HCP) knowledge and understanding. 3. Establish and disseminate clear guidance for treating JHS/EDS-HT, including assessment, referral, & complications e.g. local anaesthetics.
Negative attitudes of HCPs towards participants e.g. disbelief, anger.	○ Interpersonal skills.	○ Psychological capability.	○ Training.	4. Training for HCPs to improve interpersonal skills.
Participant fear of doctors/treatment/accidental injury. Examples: ○ Fear of being injured accidentally ○ Negative experiences (embarrassment, humiliation)/disbelieved.	○ Skills: cognitive and interpersonal. ○ Emotion: Fear.	○ Psychological capability. ○ Automatic motivation.	○ Patient education, advocacy training.	5. Training for patients focusing on advocacy, assertiveness and communication skills, to 1) reduce anxiety and 2) improve interpersonal communication of their needs to HCPs and in hospital settings.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Unsuccessful physiotherapy due to poor proprioception in JHS/EDS-HT.	○ Skills: Ability (of participant to complete physiotherapy exercises).	○ Physical capability	○ Training.	6. Training for regarding physiotherapy techniques that recognise and accommodate poor proprioception, e.g. exercises using a mirror for reference. 7. Training for healthcare professionals (HCPs) encouraging patients with JHS/EDS-HT to use a mirror when completing exercises.
Fear of potential pain/injury. Examples: ○ Cautious attitudes to avoid injury. ○ Perceived lack of control over own body.	○ Beliefs about consequences. ○ Emotion: Fear. ○ Beliefs about capabilities: Perceived behavioural control.	○ Reflective motivation. ○ Automatic motivation. ○ Reflective motivation.	○ Education, persuasion, modeling. ○ Persuasion, incentivisation, coercion, modeling, enablement.	8. Educational programmes for patients with JHS/EDS-HT, with a focus on self-help and coping strategies for injury or pain. 9. Persuasion of capability regarding physical ability. 10. Educational examples of modelled behaviours e.g. avoidance of catastrophizing and kinesiophobia.
Fluctuating nature of condition. Examples: ○ Good on some days, bad on others. ○ Hard to predict whether participants will be able to achieve goals.	○ Environmental context and resources: person x environment interaction. ○ Behavioural regulation: self-monitoring.	○ Physical opportunity. ○ Psychological capability.	○ Training, restriction, environmental restructuring, enablement. ○ Education, training, modeling, enablement.	11. Training in pacing skills to improve boom/bust cycle of activity and reduce flare-ups in symptoms and need for excessive rest time. 12. Restrict tiring, stressful or activities with a high risk of accidental injury. 13. Model pacing behaviours; planning for setback management.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Limited social participation due to symptoms. Examples: ○ Reduced mobility compared to others. ○ Reduced ability to participate socially compared to others.	○ Social influences: comparisons/ social norms.	○ Social opportunity.	○ Restriction, environmental restructuring, modeling, enablement.	14. Restructure physical environment and made modifications to reduce mobility difficulties. 15. Using behavioural modeling to show patients with JHS/EDS-HT how to communicate their needs to others in social situations.
Depression/low mood/distress. Examples: ○ Restrictions to participants' lives resulting from JHS/EDS-HT symptoms. ○ Restricted mobility. ○ Needing to plan carefully due to symptoms- losing spontaneity. ○ Issues with intimacy and sex.	○ Emotion: Negative affect.	○ Automatic Motivation.	○ Persuasion, incentivisation, coercion, modeling, enablement.	16. Use of positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped.
Restrictions to work experiences and education.	○ Interaction between person and environment.	○ Physical opportunity.	○ Training, restriction, environmental restructuring, enablement.	17. Environmental restructuring: advice from a workplace occupational therapist regarding how to restructure the environment to best meet patients' needs, and enable them to achieve their goals effectively.
Need for help, care and support from family. Examples: ○ Feelings of guilt, or of being a burden to family members.	○ Social support. ○ Emotion: anxiety and negative affect.	○ Social Opportunity ○ Emotion: Automatic Motivation	○ Restriction, environmental restructuring, modeling, Enablement. ○ Persuasion, incentivisation, modeling, enablement	18. Modeling narratives that emphasise independence from family members. 19. Environmental restructuring and enablement: altering the physical environment, with occupational therapy input, in order to achieve tasks independently. 20. Joint sessions with OT input and significant other e.g. partner.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Social stigma. Examples: ○ Judgements of others ○ Hiding JHS/EDS-HT from others ○ The idea that JHS/EDS-HT would be easier to understand if it was a visible disability. ○ Difficulties keeping up compared to others without JHS/EDS-HT.	○ Knowledge. ○ Social influences: social pressure and social comparisons.	○ Psychological capability ○ Social opportunity	○ Education, training, enablement. ○ Restriction, environmental restructuring, modeling, enablement.	21. Communication training for participants to 1) improve acceptance of condition and self-confidence in order to 2) explain and improve disease knowledge in others,
Invisible nature of JHS/EDS-HT. Examples: ○ Needing accessible seating ○ Using blue badge space	○ Social influences: social norms.	○ Social opportunity	○ Restriction, environmental restructuring, modeling, enablement.	22. Enablement of those needing accessible seating or parking e.g. Transport for London (TFL) Blue Badge scheme, council blue badge scheme.
Embarrassment. Examples: ○ Isolation/alienation from others. ○ Anger. ○ Frustration.	○ Emotion: Negative affect, alienation, stress.	○ Automatic Motivation	○ Persuasion, incentivisation, coercion, modeling, enablement.	23. Use of positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped.
Negative feelings about own body. Examples: ○ Being young but feeling old. ○ Feelings of detachment. ○ Wanting to be normal. ○ Impact of JHS/EDS-HT on masculinity. ○ Negative attitudes towards self. ○ Perceiving body as 'weird'.	○ Social /professional role and identity. ○ Social role: Identity.	○ Reflective motivation	○ Education, persuasion, modeling.	24. Education regarding positive body image. 25. Examples of first-person narratives regarding body changes with EDS.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Participant fear of decline/catastrophizing.	○ Knowledge- illness representation as degenerative. ○ Emotion: Fear.	○ Psychological capability ○ Automatic motivation	○ Patient education. ○ Persuasion, incentivisation, coercion, modeling; enablement.	26. Education for patients addressing knowledge and management of JHS/EDS-HT, pain control and self-help measures, fears about decline.
Fear of unknown situations. Examples: ○ Fear of trying new social situations. ○ Feelings of lack of control over body/environment.	○ Beliefs about consequences. ○ Beliefs about capabilities. ○ Control - of social environment. ○ Perceived competence.	○ Reflective motivation	○ Education; persuasion, modeling, enablement. ○ Persuasion, incentivisation, coercion, modeling, enablement.	27. Persuasion- emphasise participant capability. 28. Modeling of potential social situations. 29. Enablement- joint protection strategies/information for when out of the house or modeling advice for social situations.
Decisions about having children. Examples: ○ Perceived reduced physical capability in raising children. ○ Fear: children will suffer JHS/EDS-HT.	○ Beliefs about capabilities. ○ Perceived competence. ○ Beliefs about consequences- anticipated regret.	○ Reflective motivation	○ Education; persuasion, modeling, enablement.	30. Improved education and training which addresses parental fears about their ability to raise children. 31. Including modeling behaviours/modified childcare behaviours. 32. Education - Potential likelihood of child inheriting JHS/EDS-HT.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Pregnancy: potential increase in JHS/EDS-HT symptom severity, potential risks of complications.	○ Knowledge ○ Self-monitoring. ○ Emotion: Fear.	○ Psychological capability ○ Automatic motivation	○ Education, training and enabling. ○ Persuasion: incentivisation, coercion, modeling, enablement.	33. Improved education, training and information for participants with JHS/EDS-HT regarding what to expect. 34. Modeling of coping strategies from mothers with JHS/EDS-HT who have had children. 35. Develop guidance templates outlining examples of increased JHS/EDS-HT symptoms and what to do, to act as a support tool.
Problems fulfilling life demands and daily activities due to symptoms.	○ Ability (reduced ability to perform household tasks or mother due to pain/fatigue). ○ Beliefs about consequences.	○ Physical capability ○ Reflective motivation	○ Training. ○ Education, persuasion, modeling.	36. Training in Occupational Therapy methods to improve physical capability with everyday tasks. 37. Education regarding consequences of overexertion and exacerbations of pain/fatigue.

Assessing the problem: which barriers and enablers need to be addressed?	Linking to TDF Domains	Relevant COM-B components	Function(s) of the intervention	Possible solutions (Behaviour Change Techniques)
Finding out more about JHS/EDS-HT: Negative/unreliable/pessimistic information.	○ Knowledge. ○ Beliefs about consequences. ○ Emotion: Fear, Anxiety, Negative affect. ○ Environmental context and resources.	○ Psychological capability ○ Reflective motivation ○ Automatic motivation ○ Physical opportunity	○ Education, training and enabling. ○ Education, persuasion, incentives and coercion ○ Persuasion: incentivisation, coercion, modeling, enablement. ○ Training, restriction, environmental restructuring, modeling, enablement.	38. Establish guidance regarding trusted, accurate sources of information for JHS/EDS-HT. 39. Identify and restrict access to unreliable information sources. 40. Enable ease of access by providing these resources within an easily located webpage or resource.
Finding out more about JHS/EDS-HT: Comparing self to others with JHS/EDS-HT on the internet (negative).	○ Social comparisons. ○ Group identity. ○ Social norms. ○ Pessimism.	○ Social opportunity ○ Reflective motivation	○ Restriction, environmental restructuring, modeling, enablement. ○ Education: persuasion, modeling, enablement.	41. Restrict opportunities to compare self to others with JHS/EDS-HT on the internet by promoting reliable sources of information about JHS/EDS-HT.

6.6 Study 3, Stage 1: Mapping existing qualitative data: Quality assurance

In order to ensure accuracy and quality in the data mapping process, the coding was discussed and checked with the supervisory team (SP, NW, TM) at predetermined stages. The results of the first stage were also presented to a Patient Research Partner (Sue Harris) to ensure the mapping outcomes were still relevant to her own experiences as someone with JHS. When coding was complete, it was refined, reviewed and approved by two researchers with expert experience in using each method of behaviour change: the COM-B (Professor Nicola Walsh) and TDF (Dr Jen Pearson).

Mapping to the COM-B domains enables an understanding of the barriers and enabling factors that affect management of JHS/EDS-HT among adult men and women. This allowed for the identification of which behaviours may need to change in order for participants with JHS/EDS-HT to manage their condition, and what would have to happen for this change in behaviour to occur. Potential interventions relating to JHS/EDS-HT self-management were identified and organised by the lead researcher, in preparation for Stage 2.

6.6.1 Study 3, Stage 2: Identifying JHS/EDS-HT intervention options.

After mapping to the TDF and COM-B in Step 1, this second stage of the process involved identifying the potential nature and content of each behaviour change intervention. A matrix of intervention functions was used by the researcher to identify which of the nine intervention functions should be utilised, based on the TDF and COM-B mapping areas identified (adapted from Michie *et al.,* 2015, p.197-201). Each section of the TDF, and COM-B is linked to particular intervention functions, so for example, a lack of knowledge of JHS/EDS-HT would link to psychological capability, and the intervention functions education, training or enablement (see Table 6.2).

	Intervention functions								
COM-B Elements	**Education**	**Persuasion**	**Incentivisation**	**Coercion**	**Training**	**Restriction**	**Environmental Restructuring**	**Modeling**	**Enablement**
Physical capability					■				
Psychological capability	■				■			■	■
Social opportunity						■	■	■	■
Physical opportunity					■	■	■		■
Automatic motivation		■	■	■				■	■
Reflective motivation	■	■						■	■

Table 6.2: COM-B and TDF mapping intervention functions matrix (adapted from Michie *et al.,* 2015 p. 201). Shaded boxes represent the intervention functions available for each of the COM-B (and TDF) mapped elements.

6.6.2 Study 3, Stage 2: Behavioural analysis presented to a focus group of key stakeholders and refined.

The intervention development focus group was held in December 2018 and provided an opportunity to discuss the content and proposed ideas for the proposed intervention. As illustrated in Table 6.1, the compiled results of the COM-B and TDF mapping and associated modifiable behaviours had given a large number of possible

content ideas for the proposed intervention and the team discussed these options in a 90-minute review of the findings.

The group included the research team (SB, SP, NW, TM), a physiotherapist with experience of knowledge mobilisation and implementation in osteoarthritis (Laura Swaithes, Keele University) and a Patient Research Partner with JHS (PRP; Sue Harris) to ensure that the materials were clear, comprehensive and relevant to the target population. Professor Nicola Walsh has significant research experience with the COM-B behavioural change framework (Hurley *et al.*, 2016).

Potential intervention options were presented in a table developed by the researcher (SB, See Appendix M). The table listed each potential intervention function under the relevant section of the COM-B, along with definitions of key terms used in the document, an overview of the TDF and COM-B including definitions of key terms, and definitions of intervention functions, or what each intervention would do. For example, the intervention function 'education' was defined as '*increasing knowledge or understanding*'. In order for participants to have a clear overview of how JHS/EDS-HT related data had been linked to the final intervention functions, a matrix was also available to group members for contextual reference, linking each qualitative JHS/EDS-HT theme, to the applicable section of the COM-B, to the relevant TDF domain, and then the corresponding intervention function, as in Table 6.1. Each of the possible intervention features highlighted during the mapping process was discussed in turn. The key themes to emerge from this focus group discussion are outlined below.

6.6.2.1 A need for clear focus on the psychosocial impact of the condition

At this early and exploratory stage of the mapping process, barriers relating to cultural, socio-economic, and environmental conditions, including healthcare services and staff, housing, social or council services (such as disability benefits or the local council disabled Blue Badge scheme), and people's work environment were also coded as part of the mapping development. This coding was in response to barriers identified at the data level, including suggestions by participants of a need for greater training, awareness and support for healthcare professionals, in order to

raise awareness and improve knowledge and thereby diagnosis rates of JHS/EDS-HT (Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016). The group felt that while many aspects of the proposed interventions were relevant to the psychosocial impact and experience of participants with JHS/EDS-HT, that there was a risk of '*drifting too far'* from the aims of the thesis.

6.6.2.2 Psychological capability

Codes in this theme related to knowledge, which can be defined as an awareness of the existence of an entity or concept (such as knowledge of JHS/EDS-HT), memory, attention and decision processes. Possible behaviours at this level included education for patients addressing knowledge about pain control, or knowledge about pregnancy. References to improving healthcare professionals knowledge and understanding of JHS/EDS-HT, including guidance for treatment, information leaflets and training to improve awareness were removed, as these were thought to be less relevant to the psychological, cognitive and psychosocial impact of JHS/EDS-HT on the individual. The need for the focus of the work to be narrowed to the individual patient level was highlighted:

> "I think with what we've been doing up until now, it's been patients, more me orientated, rather than talking about, 'What can the doctor do?', or, 'What can a physio do?', 'what can somebody else do?'"
>
> [Sue Harris, Patient Research Partner]

The suggested item ""*Education for patients* focusing on advocacy, assertiveness and communication" was changed to "*training for patients*", as it was queried whether a better focus on skills development and training would be more appropriate:

> "Skills development and training, rather than education or improving knowledge. In terms of managing the fears and so on…[skills development training is] different, knowing what to actually behaviourally do, or how to cognitively cope with something"

[Tim Moss, PhD Supervisor]

The group agreed that improving skills would be more effective for patients with JHS/EDS-HT to learn skills relating to advocacy and communication, rather than just improving patients' knowledge.

6.6.2.3 Physical capability

Physical capability refers to an ability or proficiency acquired through practice, such as interpersonal skills. As with the prior discussions, a number of the mapped items in this column focused on improving knowledge and training those around the patient with JHS/EDS-HT. For example, educating physiotherapists regarding how to recognise and accommodate poor proprioception.

One physical capability recommendation focused on training for pacing skills, "*to improve boom/bust cycle of activity and reduce flare-ups in symptoms and need for excessive rest time"* . The requirement for this to be recognised instead as a *psychological* capability, such as people with JHS/EDS-HT pacing their activities in light of thoughts about obligations was highlighted. For example, participants in a flare of symptoms feeling socially obliged to complete activities due to feelings of guilt (Schmidt *et al.*, 2015).Therefore, the decision was made to move it to the psychological capability column:

> "I find that if I'm on a good day I just go hell for leather [with ironing]. I know that I don't get it done on a good day, I don't know when the next good day's going to be… my head's saying, 'I need to get this done'. On the other hand I've got thoughts like, 'Don't be stupid, you'll be wiped out.'
>
> [Sue Harris, Patient Research Partner]

The necessity for patients to be able to access reliable information was also discussed, but it was felt that this would be a better fit under "Physical opportunity" rather than "physical capability"; "*Enable ease of access to reliable information*

within an easily-located webpage or source", as this intervention focuses on participants' opportunity to access information.

6.6.2.4 Physical opportunity

This theme relates to any circumstances of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour (Michie *et al.*, 2015). By this point in the focus group discussion, many proposed intervention items under this heading were duplicates or very similar to other intervention options already discussed. These were merged with others or deleted. However, the intervention options relating to reliability of information were still valid:

> "'Identify and restrict access to unreliable information sources.', So rather than that, maybe giving people the skills to appraise whether information is acceptable or not, or is accurate? So, something somebody says on Facebook, is that likely to be as accurate a resource as the HMSA website?"
>
> [Sarah Bennett, Principal Investigator]

In light of this, rather than *physically* restricting an individual's access to a website (which was acknowledged by the group, may be difficult to achieve), it was suggested that interventions were put in place to "*safeguard people with JHS/EDS-HT from negative or unreliable information, by identifying and restricting access to unreliable information, and enabling easier access to reliable information within an easily-located webpage or source*". Sue described how she was also able to use more reliable information sources to educate her GP, who had not been aware of JHS/EDS-HT:

> "Until I found out about the HMSA, there wasn't much out there in the way of books, and things like that. Claire Smith wrote her book, which gave a lot of information in almost layman's terms, which made it easier, and then I passed them to my physio, I then had to pass on to my GP, and then since that he's been able to understand the condition a lot easier."

[Sue Harris, Patient Research Partner]

6.6.2.5 Social opportunity

Social influences are interpersonal processes that can cause individuals to change their thoughts, feelings or behaviours. These influences were categorised as being related to social comparisons (comparing themselves to others), perceived social pressure (from other members of society) and social norms (collective representations of acceptable group behaviour). This theme examined people's interactions in social environments and JHS/EDS-HT.

Ideas for interventions under this heading also focused on restructuring the physical environment, including making modifications to their surroundings to reduce mobility difficulties. The fact that the physical environment could not always be changed to better support the person with JHS/EDS-HT was considered:

> "You're not going to make stores put in automatic doors, you're not going to make stores put ramps in, to make it easier for people to get in and out, just to make it easier for people to go shopping."

[Sue Harris, Patient Research Partner]

Therefore, the need for people with JHS/EDS-HT to have confidence in asking others for help and communicating their own needs was highlighted as an important factor:

> "So that would be kind of creating, the supportive environments around you? Maybe managing the people around you? Because managing doesn't always mean the big environment, it means just where in which you are situated. So yeah, being able to manage your friends, your family… it's around being able to express your needs, and your requirements. Things like, knowing how to ask for help."

[Nicola Walsh, PhD Supervisor]

Sue agreed:

> "It's about knowing who you're with, and knowing who you can say, 'hold on, I can't go that fast, you slow down.' Or, 'I'll try and compromise and go a bit faster but that's just my situation."
>
> [Sue Harris, Patient Research Partner]

Participants' ability to communicate and advocate for their own requirements was highlighted in the intervention options: "*Behavioural modeling examples to show how to communicate your needs to others in social situations*", and, "*Modeling narratives that emphasise independence from family members in completing daily tasks."*

6.6.2.6 Automatic motivation

Automatic motivation is comprised of two TDF domains: emotion, and reinforcement and reward. Emotion can be defined as a complex reaction pattern involving experiential, behavioural and psychological elements, by which the individual attempts to deal with a personally significant matter or event. For example, fear was the most commonly coded TDF domain during the mapping process, and can be linked to catastrophising behaviours. The need for learning to be covert, such as modelled behaviour was discussed by the group:

> SB: [Modeling] seems to be a better way of promoting coping, rather than going; 'Well, here is a leaflet and have to do these things', [Instead it's] People… saying 'I had the same problem as you, but I did these things, and now it's okay.'
> TM: So, rather than forcing things… it's just allowing it to <u>seem</u> to happen.
>
> [Tim Moss, PhD Supervisor]

Behavioral modeling involves providing an example of behaviour for people to aspire to or imitate. Self-efficacy (the confidence to overcome challenges and maintain

desired behaviours) can be improved by the observation of successful behaviours performed by others, as in behavioural modeling (Bandura, 1997). As increases in JHS/EDS-HT symptoms have been associated with poor self-efficacy (Rahman *et al.*, 2014, Grahame, 2009), it was agreed that modelled behaviours for patients with JHS/EDS-HT would be a more effective proposed intervention.

6.6.2.7 Reflective motivation

Women in both Study 1 and 2 described their body as 'weird' or 'useless'. Some talked of feelings of detachment, that the body they saw in the mirror was not how they perceived themselves, or their identity, to be. Others talked about how, despite being aged young, because of the constant pain and injury they experienced as a result of their JHS/EDS-HT they often felt like they were living in the body of a much older person.

Suggested interventions under the reflective motivation category focused on body image. Two proposed interventions, "*education regarding positive body image*" and "*first person modeling narratives regarding body changes with EDS*" were merged and refined, to: "*education to manage beliefs and perceptions about body image*", as it was felt that the beliefs would be the main focus of any intervention; "*but it's the belief that you want to think about, what is going to have to* [change]" (NW).

During the process of discussion, the focus group actively discussed and deliberated over the correct wording and definitions for each potential intervention function, while being mindful to keep the intended focus on individual self-management of JHS/EDS-HT. By excluding a small selection of potential behaviour change interventions, this enabled the process to continue to focus on self-management of JHS/EDS-HT at the individual, patient-driven level. The categories were refined by the researcher and updated in light of the group discussions (Appendix N).

Study 3, Step 3- Identifying delivery and implementation opportunities: Feedback from participants with JHS/EDS-HT using a modified Nominal Group Technique (NGT)

Data from Step 2 regarding the potential intervention options was presented to people with JHS/EDS-HT, for review and feedback regarding the acceptability and feasibility of the proposed intervention options, using a modified face-to-face NGT method. Two modified NGT focus groups were conducted, one in Bristol and one in London. Focus groups were conducted in easily accessible rooms, with participants arranged in a semicircle with a good view of the data projector screen. Participants were provided with Turningpoint Responsecards, copies of the Participant Information Sheet (for reference, Appendix O) and a copy of the COM-B definitions and topic guide (Appendix Q).

6.7 Participant recruitment

The study was advertised to people with JHS/EDS-HT via two online sources; The Hypermobility Syndromes Association (HMSA) and Ehlers-Danlos Support UK (EDS-UK) using an online advertisement inviting eligible participants to email the principal investigator if they wished to take part (Appendix R). Those making contact were assured that all information was to remain confidential to the research team, and to follow a password-protected Qualtrics link if they wanted to participate. Qualtrics (2017, Qualtrics.com, Washington USA) is an automated survey development system that allows for data collection from any participant with an internet connection and the survey password. On expressing an interest in taking part by clicking an emailed Qualtrics link, prospective participants were presented with an information sheet to read before deciding whether or not to participate (Appendix O).

Informed consent was obtained via participants signing the online consent form using their initials. Prospective participants were then asked for basic demographic information (name, age, gender, ethnicity, support group membership, diagnosis) and were screened for self-reported generalised joint hypermobility using the Hakim & Grahame Five-Point questionnaire (Hakim & Graham, 2003, see Appendix S).

6.7.1 Generalised Joint Hypermobility

Participants were screened using their Hakim & Grahame (2003) Five-Point self-report questionnaire to screen for clinically significant hypermobility, as in previous chapters. An affirmative answer to two or more questions indicates hypermobility, and in this study phase, participants with a score of two or greater were accepted, whereas those with a score of less than two were rejected.

Inclusion criteria: Participants with JHS/EDS-HT: Aged >18 years, score 2 or more on the Hakim and Grahame (2003) Five-Point test for generalised joint hypermobility, with a self-confirmed diagnosis of JHS/EDS-HT; not diagnosed with any other subtype of EDS; able to understand and communicate in English and give informed consent.

Exclusion criteria: Failure to meet any items outlined in the inclusion criteria.

6.7.2 Original plans to recruit a representative sample of healthcare professionals

Initially, there were plans to gain feedback from approximately 3-8 healthcare professionals from a variety of disciplines, including rheumatologists, nurses, podiatrists, physiotherapists and GPs. Ideally, as recommended by Michie and colleagues (2015), these healthcare professionals would have been frontline staff with direct, empirical experience of managing and treating adults with JHS/EDS-HT.

By involving healthcare professionals in the NGT process, this would have added the benefit of first-hand information to be gathered from those working in the clinical areas most likely to encounter and treat patients with JHS/EDS-HT, and therefore those most likely to be involved in the delivery of any proposed intervention. This would have consequently improved the relevance of these findings to clinicians and clinical practice. The NGT is a very time-efficient method as a single face-to-face occurrence produces a great deal of useful information in a short space of time, a significant consideration for active healthcare professionals (Harvey and Holmes, 2012).

However, in the course of recruitment the option to recruit a sample of healthcare professionals was not possible. Although a small number of healthcare professionals responded, due to time constraints and a lack of a wider response, the decision was made in consultation with the supervisory team to focus the efforts of the present study on patient responses, with the possibility of following up with a broad and representative sample of multidisciplinary healthcare professionals as part of post doctoral work at a later date. An additional consideration supporting this decision was the observation that all work to this point in the PhD had been focused on those with JHS/EDS-HT and their own experiences, not healthcare professionals.

6.7.3 Participant characteristics

A total of 9 participants (all women) with an average age of 42 years (range 28- 57), all with self-confirmed diagnoses of JHS, EDS-HT, EDS-III or HSD were recruited into two modified NGT focus groups. Seven participants were from the South-West of England, one from the Midlands and one from the North-East. These were held in Bristol and London, on dates and times voted upon as most convenient to participants using DoodlePoll, a meeting schedule organiser platform. Eight participants attended the Bristol focus group, and one participant attended the London focus group. Six participants who had accepted invitations to participate in the London focus group were unable to attend on the day, due to childcare commitments, illness, and problems accessing the London Underground in hot weather. Details of participant demographics are presented in Table 6.3.

As only one participant was able to attend the London focus group, every effort was made to allow her to elaborate upon her answers earlier in the process, during the first stage of the process, which is usually a silent consideration of individual ideas when in a group setting. This gave the participant the chance to voice and discuss her views, experiences and reasoning for her choices less formally than in a stricter NGT format. While these stages are typically a silent contemplative stage, the participant expressed that she preferred the chance to talk and work

through her ideas and suggestions for new content, and felt that she may had been more bold with her views and opinions than she may have been in a group setting.

Table 6.3: Participant demographics for attendees of both focus groups in Study 3 (n=9)

ID	Pseudonym	Age	Gender	Ethnicity	Diagnosis	Year first diagnosed	Five-point score*
001	Helen	43	Female	White	JHS & HSD	2015	3
002	Alex	41	Female	White	JHS & EDS-HT	2018	3
003	Kelly	57	Female	White	EDS-III & EDS-HT	1998	5
004	Kris	25	Female	White	JHS	2002	5
005	Jody	51	Female	White	JHS & HSD	2012	3
006	Heather	39	Female	White	JHS	2018	4
007	Elsa	34	Female	White	JHS & HSD	2016	5
008	May	57	Female	White	JHS	2013	2
009	Julie	28	Female	White	JHS & HSD	2015	4

*Five Point Hypermobility Score, where scores ≥2 indicate hypermobility (Hakim & Grahame, 2003).

Abbreviations: EDS-HT= Ehlers-Danlos Syndrome Hypermobility Type, EDS-III= Ehlers Danlos Type III, an earlier diagnostic term for EDS-HT, HSD = Hypermobility Spectrum Disorder, JHS= Joint Hypermobility Syndrome

6.8 The Modified Nominal Group Technique (NGT) Process

A nominal group technique (NGT) method was chosen due to its benefit gaining reliable qualitative information from expert participants within a face-to-face focus group (Delbecq *et al.*, 1975). The NGT is a highly structured group process that involves equal participation and input from all participants (Harvey and Holmes, 2012). The structured method also ensures that one or more participants cannot dominate the discussions, as can occur in focus groups (Mcmurray, 1994). As the first stages in the NGT method involve silent individual consideration of ideas, while the participants are working in a group environment they are actually working individually. Participants are therefore a group by name only, this is why the process is termed a *Nominal* Group Technique.

Collaborating through the NGT method has been found to increase stakeholders' perceived ownership of the ensuing research, and has been used to establish national research priorities in clinical care (Vella *et al.*, 2000) including research priorities for Human Immunodeficiency Virus (HIV; (Haukoos *et al.*, 2009), palliative care in people with intellectual disabilities (Tuffrey-Wijne *et al.*, 2007) and supporting women with rheumatic diseases through pregnancy, birth and early parenting (Phillips *et al.*, 2018).

More relevantly, the NGT process has also been found to be a reliable method for prioritising behavioural interventions. Studies have included prioritising interventions to manage polypharmacy in residential care facilities (Jokanovic *et al.*, 2017). In this example, participants were a purposive sample of stakeholders, involving clinicians, researchers, managers and representatives from consumer, professional and health policy organisations, who were asked to devise and prioritise 16 potential interventions down to 6 preferred interventions (Jokanovic *et al.*, 2017). Likewise, a modified NGT method was used to prioritise target behaviours for research in diabetes using input from a range of healthcare professional, patient and policy stakeholders (Mc Sharry *et al.*, 2016).

To ensure adequate time for participant discussion, two modified NGT focus groups were conducted in April and May 2019 and notes were taken by a member of the research team with experience facilitating a number of research focus groups

(SP). The recommended size of a NGT is between five and ten participants, therefore a proposed sample size of between 7-10 participants for each group was considered sufficient. With more than ten participants there was increased risk that some participants would not get the opportunity to contribute their views, and that individual participation may be harder to achieve and monitor (Ritchie and Lewis, 2003). The NGT focus group was proposed to last between 3 and 4 hours. The NGT process was recorded using a digital Dictaphone, transcribed verbatim and any identifying information removed to ensure participant confidentiality. Participants' contributions using Turningpoint ARS were saved within the software before being converted for tablature and evaluation using Microsoft Excel.

The NGT comprises four key stages: silent generation of ideas, a round robin sharing of ideas, clarification and discussion, and voting (this can be ranking or rating the items, (Delbecq *et al.*, 1975), (Mcmillan *et al.*, 2016). The NGT protocol was adapted from Potter et al (2004) and the stages involved in the process are described below (Potter *et al.*, 2004).

6.8.1 Sending information to NGT participants in advance

Before the study commenced, prospective participants were sent information about the modified NGT process one week in advance of the study (Appendix O and Q). Relevant information regarding the twenty shortlisted behaviour change intervention options for JHS/EDS-HT management from Stage 2 and key definitions was emailed to prospective participants in advance of the face-to-face modified NGT study. This was the same pack of information that participants received on the day of the NGT (see Appendix Q). The email also invited participants to ask questions about any area of the study or wording that was not clear. This gave participants ample time to consider all the behaviour change options, formulate ideas and have the opportunity to ask any questions and gain clarification in advance of the process.

6.8.2 Introduction to the NGT study

At the start of each face-to-face meeting, participants were provided with an initial introduction and explanation of the process and purpose of the session. Session ground rules were established and explained, and participants given a short explanatory presentation, with an overview of research conducted into hypermobility by the candidate to date, and how Study 1 and Study 2 had been mapped onto the TDF and COM-B in a behavioural analysis. Participants in both NGT groups were particularly positive and engaging at this stage, and keen to ask questions about the findings of previous studies and what other avenues of research are currently being conducted into JHS/EDS-HT in the UK.

Again, as with the qualitative telephone interviews used in Study 2 of this research, the candidate made efforts to reduce the power imbalance often seen in qualitative research by disclosing that she also had JHS/EDS-HT, but stressing that her own experiences were likely to be different, and that it was the participants' views and opinions that were important.

6.8.3 NGT Step 1: Round-robin generation of ideas and modifications for the present study

The NGT method traditionally involves a 'round-robin' participant generation of ideas at one of the first stages in the process. This study used a modified NGT as data had already been gathered for the mapping process in Stages 1 and 2. In these stages, data from the Study 1 systematic review and Study 2 semi-structured interviews with adults who have JHS/EDS-HT was mapped onto the TDF and COM-B models to produce a series of behavioural change interventions. Therefore, rather than the primary focus being to generate original ideas, participants were invited to rank the previously identified and refined behaviour change intervention options by importance. However, in case of any additional ideas or contributions, participants were invited to share any further ideas for behaviour change interventions they would like to add at the discussion stage of the process.

6.8.4 NGT Step 2: Individual silent ranking of ideas

In the second step of the NGT, participants were provided with the same information pack that they had received prior to the NGT (Appendix Q), and a Turningpoint ResponseCard keypad; devices with numbered keys enabling them to individually and anonymously vote for their chosen options. At this stage, participants were offered the option of using a pen to press the buttons on the Response Card, in the case of reduced manual dexterity. In both NGT focus groups, participants were happy to respond without assistance.

Participants were asked to respond to each of the 20 behaviour change interventions while considering the proposed question:

"Which of these factors would you consider important in a JHS/EDS-HT-related intervention?"

A series of slides featuring the outcomes identified in Stage 2 were presented to participants, and they were asked to respond individually using their TurningPoint ResponseCards. For each of the 20 behaviour change interventions, clarifying information (such as the underlying themes and features of the qualitative data informing the creation of the behaviour change intervention), and definitions of each term used (for example, 'education' was defined as '*increasing knowledge or understanding*') were made clear, and participants given the option to ask any clarifying questions before each behaviour change interventions was voted upon. Participants could respond using a four-item Likert scale; from 1 = Not important/not applicable; 2 = Somewhat unimportant; 3 = Somewhat important; and 4 = Very important.

The need to not discuss their ideas with each other at this stage and to respond individually was emphasised and participants assured that later stages in the process would give ample time and consideration to anything they would wish to add to the process. Participants were encouraged to make a note of anything they may wish to add to the twenty behaviour change interventions, for consideration in Stage 3.

One criticism of the COM-B and TDF BCW process is the complexity of the language used, and a reliance on strict terminology and definitions. Although

participants had been provided with a list of key terms and definitions of words used in this phase of the study as part of the NGT process, there was some concern from the researcher that participants may misinterpret or fail to understand some of the terms, or have a different conception of a term, compared to the official definition. Therefore, to ensure good understanding, participants were given thorough verbal explanations regarding the definition of each term used by the facilitator (SB), and participants were invited to ask any clarifying questions before voting to ensure understanding of all the terms used in each intervention. A copy of this can be found in Appendix Q.

6.8.5 NGT Step 3: Sharing ideas

The third step in the NGT process involved participants proposing any additional ideas in turn, around the group, without debate, until all rankings had been recorded (Potter *et al.*, 2004).

Feedback from participants was typed verbatim by the candidate (SB) onto the Powerpoint presentation visible to all participants by means of a data projector, to ensure all ideas had been recorded, to give visual feedback to participants, and to keep an accurate record of the process. Participants' ideas were modified by the NGT group facilitators (SB & SP), with input on wording and general suggestions regarding the content of each idea from the group. Care was taken to match participants' new suggestions with agreed definitions and methods of behaviour change, as set out by Michie and colleagues (Michie *et al.*, 2015) to ensure as close a fit with the 20 identified options as possible.

When the refinement of new behaviour change techniques was complete, participants were asked to vote on each new idea, using their TurningPoint ResponseCards and the same 4-item likert scale as in Stage 2; from 1 = Not important/not applicable; 2 = Somewhat unimportant; 3 = Somewhat important; and 4 = Very important.

6.9 Stage 4: Group discussion

6.9.1 Discussion and prioritisation of items

The fourth step involved a group discussion, where participants were invited to consider their top two preferred intervention options. Participants were given 30 minutes to individually consider their options before feedback to the rest of the group. The slide for this stage asked; '*From the items discussed, which 2 items would you prioritise as most important in a JHS/EDS-HT-related intervention?*' This prioritisation also involved the new ideas shared by participants in the previous stage. Participants were asked to consider the appropriateness, acceptability, feasibility, perceived limitations and proposed solutions relating to a JHS/EDS-HT intervention (see Table 6.4 below). For each of their two chosen preferred intervention options for managing JHS/EDS-HT, participants were asked to consider them in relation to these criteria and to make a practical judgement ((Michie *et al.*, 2015), p. 20).

Acceptability can be defined as the degree to which different stakeholders judge the proposed intervention to be appropriate (Michie *et al.*, 2015). The concept of acceptability is a key consideration when designing, evaluating and implementing healthcare interventions and is considered necessary condition for the effectiveness of an intervention (Sekhon *et al.*, 2017). In order to be implemented effectively, the intervention must be acceptable to all stakeholders, including deliverers of the intervention (e.g. researchers or healthcare professionals with experience treating patients who have JHS/EDS-HT) and recipients (patients with JHS/EDS-HT, (Diepeveen *et al.*, 2013).

Feasibility, in addition to acceptability and appropriateness, (Weiner et al., 2017) which, when affirmative, are often considered good indicators of the success of an intervention (Proctor et al., 2011). In this case, participants were given the examples '*Would the intervention be achievable, not too much effort or a burden to complete?'.* In asking these questions, it can be ascertained whether the behaviour change option presented is possible, doable and easy to achieve or complete (Weiner *et al.*, 2017). For example, can the intervention be delivered as designed, or would it require additional staff training, or a larger building space.

Each participant was encouraged to contribute in a 'round-robin' format led by the facilitator (SB) with other members of the group discussing each of their chosen items. Group discussion again encouraged participants to identify any further support they felt would be beneficial, which may not have been considered in the original Stage 1 COM-B and TDF mapping process.

Participants were further asked about how they would prefer the implementation to be delivered, and whether the proposed option (such as face-to-face delivery of training) was achievable in light of the above criteria. Participants' views were shared and discussed as a group to reach consensus. In the case of the single participant in the London focus group, the participant discussed with the facilitators (SB & SP) to reach a conclusion.

Table 6.4: The proposed criteria for participants to appraise their two chosen behaviour change interventions, and associated definitions (adapted from Michie *et al.,* 2015 p. 49).

Criteria	Definition
Appropriateness	*Is the intervention proposed appropriate?* Would the proposed intervention be of clinical benefit to the person with JHS/EDS-HT, would the expected health benefits exceed any negative consequences?
Acceptability	*Is the intervention proposed acceptable?* The extent to which different stakeholders (such as the patient population with JHS/EDS-HT, healthcare professionals with experience treating JHS/EDS-HT) can judge the proposed intervention as appropriate. For example, participants with JHS/EDS-HT may want fast-track treatment for certain issues, but this may not be the same view held by healthcare

	professionals.
Feasibility	*Would the intervention be achievable, not too much effort or a burden to complete?* For example, can the intervention be delivered as designed, or would it require additional staff training, a larger building space etc.? Would the proposed interventions be cost-effective to deliver?
Perceived limitations	*Are there any perceived limitations, such as financial or time limitations?* These potential limitations may relate to the cost, or affordability of an intervention. For example participants may suggest individualised one-to-one drop-in support with a specially trained physiotherapist for a year, but this idea as it stands may be too expensive for implementation in an NHS setting. In addition, an intervention must be socially acceptable to participants, and there must be sufficient time.
Perceived solutions	*If there are limitations, can you think of any solutions to these?* Any potential answers or resolutions to any limitations or barriers to implementing the proposed intervention. Would the proposed intervention improve care for participants with JHS/EDS-HT?

Nominal Group Technique Protocol

1. **Initial introduction and explanation:** Participants welcomed and the purpose and procedure of the focus group NGT session was explained. At this stage, participants were welcome to ask any clarifying questions about the options presented **(5 minutes)**.

2. **First individual ranking of ideas**: Participants were provided with potential intervention options via Microsoft Powerpoint. For reference, the question to be addressed was stated: "*Which of these factors would you consider important in a JHS/EDS-HT-related intervention?"*.

   Participants' could respond to each intervention option using a Likert scale (1 = *Not at all important*; 2 = *Somewhat unimportant*; 3 = *Somewhat important*; 4 = *Very important*). There was also space to record any new ideas. During this period, participants privately rated the items in order of preference using Turningpoint Responsecards. This phase was individual, participants were advised not to consult each other or discuss their views **(45 minutes-1 hour)**.

3. **Individual sharing of additional ideas:** Participants could share any additional ideas they had generated with the group. The facilitator recorded each idea verbatim onto a PowerPoint slide visible to the group via a data projector. The individual feedback process continued until all participants had presented their ideas. There was no discussion with other group members at this stage **(15-30 minutes)**.

Lunch break (1 hour)

4. **Group discussion:** Participants were invited to select their top two most important items from the 20 possible optionsEach behaviour change intervention was discussed in terms of their opinions regarding the appropriateness, acceptability, feasibility, perceived problems and solutions relating to a JHS/EDS-HT intervention. Each person was allowed to contribute and discussion was mediated to ensure fair time allocation to each idea **(35-40 minutes).**

5. **Final voting and ranking:** The ideas were voted on and prioritised in relation to the question. Immediate results were available in response to the question posed. The meeting concluded after having ranked all the items a second time **(30 minutes).**

Figure 6B: The NGT protocol adapted from Potter *et al.,* (2004).

6.9.2 Commenting on London NGT Focus Group additional ideas

An ethics amendment was applied for, and approved by the University of the West of England Faculty Research Ethics Committee (HAS.18.03.128, 11th June 2019, Appendix T) inviting participants who had taken part in the Bristol NGT focus group to comment and vote upon the proposed additional ideas suggested by May in the London NGT focus group. However, as only two of the eight participants in the Bristol group offered their responses, this was not enough data to conclusively give an additional second voting. As a result, this second voting data was not included in the analysis, but has been included in the results (Table 6.4).

6.9.3 Stage 5: Voting and ranking

Lastly, participants were invited to re-rank the 20 proposed intervention options and any new options identified at Stage 2. An example of the stages of the NGT, with approximate time allocated, is illustrated in Figure 6B.

6.10 Results of the modified Nominal Group Technique focus group

6.10.1.1 Justification of ranking and consensus scores

Before data collection began, it was agreed that participants' agreement was to be calculated by combining likert scale scores for high (3 = Somewhat important; and 4 = Very important) , and low total scores (1 = Not important/not applicable; 2 = Somewhat unimportant). For example, if all 9 participants had ranked 3 = Somewhat important; or 4 = Very important, then the total high consensus score would be 9, giving a higher rank than if participants scores had been lower for that item (scores of 1 = Not important/not applicable, or 2 = Somewhat unimportant) (Waserman *et al.*, 2010).

Consensus was reached when agreement was ≥89%, or scores of 8/9 or higher. Items with the highest total score (combined scores of 9 or 8) in the second round of NGT ranking were prioritised for intervention content. Although other examples of NGT prioritisation have used cutoffs of 80% (Waserman *et al.*, 2010), a cutoff of 7/9 (78%) gave a participant intervention prioritisation list of 20 items. A pragmatic decision was made for the purposes of the thesis to raise the consensus

level to 8/9 (89%) in order to focus on the top 14 items. Future postdoctoral work could explore all 20 items for prioritisation, both with further groups of participants and with healthcare professionals.

6.10.2 Potential interventions in the self-management of JHS/EDS-HT

All participants completed the survey and ranked each of the 20 interventions twice; before and after a group discussion (Table 6.4). As explained in the methods section of this chapter, participants scored the 20 options presented and any additional options using their TurningPoint ResponseCards and the same 4-item likert scale as in Stage 2; from 1 = Not important/not applicable; 2 = Somewhat unimportant; 3 = Somewhat important; and 4 = Very important. These scores, before (round 1) and after the discussion of participants preferred options (round 2), and the combined scores of each item are presented in Table 6.5. Participants scores on Round 2 of the NGT were then used for prioritisation of items, as participants had been given a chance to rate, discuss and re-rate items.

Table 6.5: Results from the Nominal Group Technique (NGT) focus group voting.

Intervention	Round 1 voting				Totals		Round 2 voting				Totals	
	1	2	3	4	LOW	HIGH	1	2	3	4	LOW	HIGH
1. Skills development training for patients focusing on advocacy, assertiveness and communication, to improve interpersonal communication of their needs.	0	0	6	3	0	9	0	1	4	4	1	9
2. Education for patients addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures, fears about decline.	0	0	2	7	0	9	0	0	1	8	0	9
5. Training in pacing skills where individuals can learn to actively manage cycles of activity and rest to achieve increased participation in daily activities.	0	0	3	6	0	9	0	0	6	3	0	9
11. Educational examples of behaviours, including self help strategies for coping with injury and pain.	0	0	2	7	0	9	0	0	2	7	0	9
16. Educational programmes with a focus on self-help and coping strategies for injury or pain.	0	0	2	7	0	9	0	0	1	8	0	9
20. Education regarding consequences of overexertion and exacerbations of pain/fatigue.	0	0	3	6	0	9	0	0	3	6	0	9
22. Education: How to evaluate information (Additional Idea 2 Bristol Group).	0	0	5	4	0	9	0	0	7	2	0	9
3. Improved education, training and information for participants regarding what to expect during pregnancy.	1	0	0	8	1	8	1	0	7	1	1	8
4. Establish guidance regarding trusted, accurate sources of information for JHS/EDS-HT.	0	0	4	5	0	9	0	1	2	6	1	8
9. Environmental restructuring and enablement: altering the physical environment, with occupational therapy input, in order to achieve tasks independently.	1	1	4	3	2	7	0	1	3	5	1	8
12. Positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped.	0	3	1	5	3	6	0	1	4	4	1	8

Intervention	Round 1 voting				Totals		Round 2 voting				Totals	
	1	2	3	4	LOW	HIGH	1	2	3	4	LOW	HIGH
15. Develop templates outlining examples of increased JHS/EDS-HT symptoms during pregnancy and what to do, to act as a support tool.	0	1	4	4	1	8	0	1	8	0	1	8
23. Education regarding how to navigate social support e.g. Blue Badge, charity support, benefits and Access to Work (ATW) or Disabled Students' Allowance (DSA) funding (Additional Idea 3 Bristol Group).	0	0	2	5	0	7	1	0	1	7	1	8
24. Enablement: Access to emotional support e.g. mindfulness, counselling, CBT or books (Additional Idea 4 Bristol Group).	0	0	2	7	0	9	1	0	0	8	1	8
6. Promote information to improve knowledge of accessible seating or parking – the Transport for London Blue Badge scheme, local council Disabled Blue Badge scheme.	0	3	3	3	3	6	1	1	4	3	2	7
7. Behavioural modeling examples to show how to communicate your needs to others in social situations.	0	3	2	4	3	6	0	2	5	2	2	7
10. To safeguard from negative or unreliable information: 1) Identify and restrict access to unreliable information sources. 2) Enable ease of access to reliable information within an easily located webpage or source.	1	1	2	5	2	7	0	2	3	4	2	7
14. Education regarding the likelihood that their child will inherit JHS/EDS-HT and signposting for support.	1	0	4	4	1	8	0	2	4	3	2	7
17. Education to manage beliefs and perceptions about body image.	0	3	2	4	3	6	0	2	5	2	2	7
21. Tailored information only when appropriate (Additional idea 1 Bristol Group).	1	0	4	4	1	8	0	2	3	4	2	7
13. Modeling of coping strategies from mothers with JHS/EDS-HT who have had children.	0	0	4	5	0	9	0	1	6	0	1	6
8. Modeling narratives that emphasise independence from family members in completing daily tasks.	0	3	3	3	3	6	0	4	2	3	4	5

Intervention: Additional participant-suggested ideas: London focus group	Round 1 voting				Totals		Round 2 voting				Totals	
	1	2	3	4	LOW	HIGH	1	2	3	4	LOW	HIGH
25. Education for others regarding JHS/EDS-HT- what it is and how it affects people (Additional Idea 1 London Group).	0	2	0	2	2	2	0	0	1	1	0	2
26. Education regarding common behaviours and lived experiences of JHS/EDS-HT, compared to others (Additional Idea 2 London Group).	0	1	1	2	1	3	0	0	1	1	0	2
27.Modeling examples from a mentor with JHS/EDS-HT (Additional Idea 3 London Group).	0	0	2	2	0	2	0	0	1	2	0	3

6.11 Results: Participants' additional self-management intervention ideas

As part of the NGT process, participants were invited to share any additional ideas they may have thought of that had not been covered as part of the COM-B and TDF mapping process that they would like to see as part of an intervention. These are detailed below, where underlined text is emphasis during speech.

6.11.1 Bristol Focus Group Additional idea 1: Tailored information only when appropriate

Participants liked the fact that many of the proposed interventions focused on patient education and providing more information to improve participants' knowledge of JHS/EDS-HT. However, some felt that they could be overloaded by information about JHS/EDS-HT:

> "I think that sometimes [patient education and information] has the opposite effect… I think there can be a lot of fear-mongering as well. So, say, for example, if I hadn't been pregnant, or had a child ... if I was being fed loads of information about things that might go wrong, you know? I think that might kick in the anxiety and that anxiety and pain for me… So. I would rather have <u>less</u> information…"
>
> [Alex, Bristol focus group]

The group discussed the need to receive tailored, supportive information about JHS/EDS-HT, rather than information regarding all potential risks:

> "I wouldn't want to turn up to the doctors and be bombarded with well, this risk, that risk, (crosstalk) I need to worry about this, worry about that ... I'd rather turn up to the doctors and they'd be like, 'Are you aware of ... And this is how we can help you manage through it. You can still have children."
>
> [Elsa, Bristol focus group]

"Prompting to say, 'Actually, this is what could happen, you know?"

[Helen, Bristol focus group]

The need for this information to be needs-based was emphasised, and depending on what the patient with JHS/EDS-HT required at the time. Participants also indicated that they wanted information provision to be holistic, and in consideration of the patient as a whole, but the recognition that this could be difficult with current treatment options was acknowledged:

"[Patient education] does need to be tailored, I think, but for it to be tailored you need to know the person, and I don't how you get around that, because often it's only one, like you only see the doctor, or health visitor, or whatever, no one looks at you as a whole?"

[Elsa, Bristol focus group]

In general, participants in Study 2 and 3 indicated that patients wanted to improve their knowledge about their condition but indicated that the information they had received about JHS/EDS-HT since being diagnosed was insufficient:

Alex: But it is quite telling though, that when you get a diagnosis you're given a pamphlet about arthritis (.) I mean, that is quite a thing, about sort of (.) The NHS and their understanding of patient education, really.
Julie: It's quite funny inside, I have one of the arthritis ones, it was like, 'Sex with arthritis,' and it was a couple of- oh, I don't know, seventy-year-olds in the front? Smiling? (group laughter) and they're just giving you all these books, and there is not anyone under the age of seventy, in any of them […] reading it you just feel like, this doesn't really apply, like, to you.

[Alex and Julie, Bristol focus group]

Participants also highlighted the fact that without sufficient information, they would be forced to look for things on the internet, an option that came with its own challenges:

"Because otherwise, you end up looking at things yourself, and that's when you're finding things that might not be applicable-"

[Heather, Bristol focus group]

6.11.2 Bristol Focus Group Additional idea 2: Education: How to evaluate information.

The development of internet-based health education and support for patients has opened up an abundance of possibility for the delivery and communication of health information to patients. Compared to those who had been diagnosed in the 1990s, participants diagnosed within the last 20 years had access to a much greater range of information than before:

"When I [was diagnosed] it was in the Nineties, and it wasn't like it is now… it was just ... 'here's a book', well, it was a paper thing, I think? From the EDS society …newsletter? So it is obviously all been vetted, they put it together ... It's not some bloke on Facebook making up a load of rubbish… So, I must admit, nowadays you go on [the internet], and it's like ... Anything, for cancer, anything, (gasps dramatically)"

[Kelly, Bristol focus group]

"It's called [Ehlers-Danlos Syndrome], DO NOT GOOGLE IT! (laughs) The information on the internet is rubbish, right?[. .] [Work colleague:] Oh, this is the condition that woman's got!' and I'm like, , No, it's NOT! That's a whole lot of bollocks you've found on the internet!'"

[May, London focus group]

Kelly and May's statements indicate the difficulties in being able to find reliable information that wasn't "*a load of rubbish*", and the risks of encountering inaccurate material that participants may find frightening. This additional intervention idea centred around being able to appraise and evaluate the wealth of information available to patients

with JHS/EDS-HT on the internet, from websites to social media platforms. Participants cited difficulties in being able to separate reliable information from unreliable or untrustworthy material, as Julie explains:

> "There needs to be like, education, on like, how to identify what is negative or unreliable information? Because sometimes they're like, 'Oh, have a look on the Internet', You know? To get some advice, but also, you need to be careful ... Anxious people can stir up a storm online, can't they?"
>
> [Julie, Bristol focus group]

Participants also recognised that some information about JHS/EDS-HT might be negative, as this was sometimes the nature of the condition:

> "I was thinking about the word negative as well? I mean, we are going to have to face some stuff that we wouldn't like to hear, at times? And just because it's negative, doesn't mean it's not important information to have? [...] I've got pelvic floor problems… Again, it would have been nice to know about the risks of pelvic floor issues [with JHS/EDS-HT]?"
>
> [Jody, Bristol focus group]

In light of this, the wording was modified to focus on improving participants' ability to appraise the information they discovered.

6.11.3 Additional Idea 3 Bristol Group: Education regarding how to navigate social support e.g. Blue Badge, charity support, benefits and Access to Work (ATW) or Disabled Students' Allowance (DSA) funding.

In view of wide reform of the UK welfare system since the 1990s, former kinds of disability payments have since been replaced by Personal Independence Payments (Roulstone, 2015). If the help that participants needed at work could not be covered by their employer making reasonable adjustments, they may be able to gain assistance from Access to Work (ATW), a

government initiative to support disabled people in the workplace with funded grants to cover the costs of practical support, specialised equipment or help getting to work, such as taxis. Participants were keen for education and support in regards to what they may be entitled to in terms of funding:

> "I've not been entitled to any benefits… but I learnt the other week that I could be entitled to Access to Work funding? [. .] I'm still ... Not optimistic about what I'm going to get! (Laughs)…but, it's something I didn't know about until three weeks ago."
>
> [Elsa, Bristol focus group]

Although many felt they may be eligible for funding, it was difficult for participants to know which benefits they may be entitled to, or how to ask for support when making an application. As Heather explained:

> "I've got a friend…she was going through the [Personal Independence Payments] benefits thing ... And she had some help… how do you even navigate that? Where do you start? Where else can I get support?
>
> [Heather, Bristol focus group]

6.11.4 Bristol Focus Group Additional Idea 4: Enablement: Access to emotional support e.g. mindfulness, counselling, CBT or books.

Participants were keen to see more support to manage the psychological aspects of managing JHS/EDS-HT, including acceptance of their condition, compared to the physiotherapy management they were usually offered:

> "Try this strategy, and try this strategy, has been more helpful for me to ... To talk through kind of, the issues, and the acceptance, and stuff, rather than actually having ... A list of things to do, you normally come away with a list of physio exercises ... You come

away with a list of medications, so I don't want to (laughs) come away with a list of like ... mindfulness exercises as well! It's hard work."

[Elsa, Bristol focus group]

6.11.5 London Focus Group Additional Idea 1: Education for others regarding JHS/EDS-HT- what it is and how it affects people.

This additional idea linked to a lack of awareness or understanding of the condition in others. The context for this idea related to a need to increasing knowledge and understanding in others. For this participant, understanding that the symptoms of JHS/EDS-HT are real and genuine was very important:

"I think [Additional Idea 1] is about expectation, so for me that's all part of the 'it's invisible, you can't see it, but it's <u>real'</u> thing."

[May, London focus group]

'How it affects people' refers to both the potential limitations placed on a person with JHS/EDS-HT, but also strengths or benefits that they may gain from their hypermobility:

"The other thing is that people will be able to lead with what they can do- their capability and their functionality…not predetermining what that person's abilities would be".

[May, London focus group]

For example, people might do certain tasks differently because they have JHS/EDS-HT, compared to other people who are not hypermobile. The inverse is also true, that there might be a different way that the general population would do something because they are not as flexible as someone with JHS/EDS-HT.

6.11.6 London Focus Group Additional Idea 2: Education regarding common behaviours and lived experiences of JHS/EDS-HT, (compared to other people who don't have JHS/EDS-HT).

This idea related to improving the knowledge and understanding of the kinds of symptoms and signs that might be typical of someone with JHS/EDS-HT, and how best to manage the impact of these signs:

> "It's a different kind of education, I think, it's not necessarily a medical intervention, it's a, 'This is the skeleton you were born with, this is the impact it might have, here's some really good ideas about how to sort some stuff out."

[May, London focus group]

For example, one 'common behavior' related to increased flexibility of the lumbar spine and hips in JHS/EDS-HT. Those with JHS/EDS-HT, due to increased flexibility did not need to crouch right down to tie shoelaces, whereas people without JHS/EDS-HT would need to bend down to tie their shoes, due to their comparative lack of flexibility. Another example given was due to increased flexibility of arms and shoulders, not needing to use buttons or zips to get clothing on or off:

> "I put zips in clothes, because other people [without hypermobility] put zips in clothes… But I don't need the zip? I don't undo the zip. I can get in and out of most things without the zip."

[May, London focus group]

> "So it's like identifying the discrepancies between the [JHS/EDS-HT] world, and the … normal connective tissue world."

[May, London focus group]

6.11.7 London Focus Group Additional Idea 3: Modeling examples from a mentor with JHS/EDS-HT.

A third additional idea related to the concept of modelled behaviours, from a mentor with JHS/EDS-HT. Modeling can be defined as providing an example of behaviour for people to aspire to or imitate. The mentor would need to be someone with whom the person with JHS/EDS-HT could interact:

> "A real person, because I think that creates two things, a touchpoint, which is a viewpoint where other people understand where you're coming from… So if you have a mentoring structure, that allows the mentors to share knowledge."
>
> [May, London focus group]

May provided an example:

> "You could have somebody that could mentor you on being able to… long-distance travel [with JHS/EDS-HT], so people quite often ask that on social media, 'I need to fly 4 hours from A to B, how do I do it?'"
>
> [May, London focus group]

The mentor would also have JHS/EDS-HT and be able to provide advice and support to participants via modeled examples of behavior. As indicated in Study 2, adults with JHS/EDS-HT discussed making friends with other people who were similar to themselves in terms of disability or physical limitation. Research indicates that people tend to trust others that are more similar to them, compared to others such as authority figures from government, the media or business, therefore the information available from a mentor would have the potential to persuade members of that shared community (Willis and Royne, 2017).

6.12 Results: Interventions rated for importance: NGT

The interventions ranked as being of the greatest importance at the end of the NGT process are outlined below. Table 6.5 indicates the list of 20 potential interventions and additional ideas generated by the Bristol (4 additional ideas) and London focus groups (3 additional ideas) and the total scores given for each item. These were then reduced to 14 prioritised interventions (total consensus scores greater than or equal to 8). Participants high consensus scores from the second phase of voting were used for prioritisation, as by this point they had been able to discuss and evaluate their reasons for prioritisation as a group.

Overall, 14 interventions were identified as important to participants in the NGT process, and these can be categorised into 4 areas; 1) education; 2) training; 3) modeling; and 4) environmental restructuring and enablement:

6.12.1 Education:

- Education for patients addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures and fears about decline.
- Educational examples of behaviours, including self help strategies for coping with injury and pain.
- Educational programmes with a focus on self-help and coping strategies for injury or pain.
- Education regarding the consequences of overexertion and exacerbations of pain/fatigue.
- Education: How to evaluate information (Additional Idea 2 Bristol Group).
- Establish guidance regarding trusted, accurate sources of information for JHS/EDS-HT.
- Templates outlining examples of increased JHS/EDS-HT symptoms during pregnancy and what to do, to act as a support tool.
- Education regarding how to navigate social support e.g. Blue Badge, charity support, benefits and Access to Work (ATW) or Disabled Students' Allowance (DSA) funding (Additional idea 3: Bristol focus group).

6.12.2 Training:

- Skills development training for patients focusing on advocacy, assertiveness and communication, to improve interpersonal communication of their needs.
- Training in pacing skills where individuals can learn to actively manage cycles of activity and rest to achieve increased participation in daily activities.
- Improved education, training and information for participants regarding what to expect during pregnancy.

6.12.3 Environmental restructuring and enablement:

- Environmental restructuring and enablement: altering the physical environment, with occupational therapy input, in order to achieve tasks independently.
- Enablement: access to emotional support such as mindfulness, counselling, CBT or books (Additional Idea 4 Bristol Group).

6.12.4 Modeling:

- Positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped.

6.12.5 Results: Participant's top 2 prioritised items

Participant's top prioritised items are shown in Table 6.6. Each participant chose their preferred first and second options for prioritization, and discussed these in terms of appropriateness, acceptability, feasibility, perceived limitations and solutions. Seven of the ten interventions (70%) were the same as those prioritised by focus group participants in the NGT process, indicating a good agreement between items prioritised at the group and individual level. Of the three remaining, Bristol focus group additional idea 1 "*Tailored information only when appropriate*" and "*Behavioural modeling examples to show how to communicate your needs to others in social situations*" were ranked 7/9 or 78% agreement. The "*London Focus Group Additional Idea 3: Modeling examples from a mentor with JHS/EDS-HT*" had a more limited response, and this is discussed above. Due to the need for a pragmatic focus on a smaller number of items these were not included in the NGT ranking.

However, an important limitation to consider is that these results are only based on the experiences to the small number of participants at this stage of the research (n=9), all of whom were women over the age of 18, resident in the UK and of White ethnicity. Therefore the claims made at this stage are only tentative. These results should be further verified with future research with a larger number of diverse participants, such as men, or participants from differing sociocultural and ethnic backgrounds in order to draw stronger conclusions. Likewise, due to differences in access to healthcare, participants from European countries or the United States with JHS/EDS-HT may give differing intervention priorities to the populations in the present study. Results from a larger population of patients, from other stakeholders with experience caring for patients with JHS/EDS-HT or from different researchers may confirm, challenge or change these results, or reach different conclusions.

Table 6.6: Participants top two prioritised items, as indicated in the NGT group discussion.

Intervention	Helen	Elsa	Alex	Kris	Kelly	Jody	Heather	Julie	May
24. Additional Idea 4 Bristol Group: Enablement: Access to emotional support e.g. mindfulness, counselling, CBT or books*.		2nd		2nd		2nd		1st	
9. Environmental restructuring and enablement: altering the physical environment, with occupational therapy input, in order to achieve tasks independently*.	1st	1st			2nd				
2. Education for patients addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures, fears about decline*.			1st		1st		1st		
12. Positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped*.							2nd	2nd	
20. Education regarding consequences of overexertion and exacerbations of pain/fatigue*.	2nd								
11. Educational examples of behaviours, including self help strategies for coping with injury and pain*.									1st
1. Skills development training for patients focusing on advocacy, assertiveness and communication, to improve interpersonal communication of their needs*.						1st			
21. Additional idea 1 Bristol Group: Tailored information only when appropriate			2nd						
7. Behavioural modeling examples to show how to communicate your needs to others in social situations.				1st					
London Focus Group Additional Idea 3: Modeling examples from a mentor with JHS/EDS-HT.									2nd

* = Interventions that also feature in participants highest-scored NGT items.

6.13 Results: Nominal Group Technique

Participants reasoning for their chosen interventions in the voting and group discussion phases of the NGT are explored below.

6.14 Elements of the proposed intervention

6.14.1 Education

All emphasised a need for good-quality patient education in managing their JHS/EDS-HT, and that this may be seen as more trustworthy when delivered by people who also have JHS/EDS-HT themselves:

> "I haven't necessarily found a huge amount of help from medical professionals, I've certainly found that most of the knowledge I've gained has been from fellow hypermobile sufferers, or EDS, people who had those diagnosis ... I tend to look more towards those sorts of people as the people who are knowledgeable"
>
> [Heather, Bristol focus group]

Patient education could include a focus on self-help and self-management strategies for managing injury, such as the use of heat, stretching and massage to manage pain, and how to adapt and combine these in order to gain the greatest benefit. During discussion, knowledge and management of JHS/EDS-HT extended to some participants learning basic human anatomy to self-manage, using self-taught physiotherapy exercises for their JHS/EDS-HT symptoms at home:

> "Because, the education never ends, you have just constantly keep going, learn how to … sort yourself out, so now I like, Google the anatomy, find out which muscle is hurting, and then look up different physio stretches… So you kind of just end up treating yourself, after a while!"

[Julie, Bristol focus group]

Interestingly, self management advice and either online or face-to-face delivery and input from someone who had JHS/EDS-HT was seen as more reliable, compared to the '*negative*' information that participants might find on the internet:

> "Figuring out stuff-… self- help, I mean this [focus group], just…chatting with other people today has been brilliant! (Laughs)… I mean, you don't often meet people, you know, who got similar experiences? I mean, you see them all on Facebook but ... It can be a bit negative"

[Kelly, Bristol focus group]

Many spoke of a need to amass reliable, accurate information about JHS/EDS-HT, and related social support (such as support from disability benefits or charities) to '*prepare'* themselves, and their children, for the possible issues they might have in the future if their condition changed, and to enable them to make the best choices about their care:

> "Yeah, because I'm the first one in my family ... with this, …I feel if I'd known stuff before, I probably would have done if you think differently, or helped differently. I feel like I'm gathering information for trying to prepare my children for the issues that they may possibly have in the future"

[Alex, Bristol focus group]

6.14.2 Training

Pacing activity, and finding a balance between exercise and rest was also cited as important to self-management in JHS/EDS-HT. Participants in Study 2 indicated that the fluctuating nature of JHS/EDS-HT meant that they often had to plan ahead and pace both their physical movements (to avoid injury) and their activities. Almost all participants in Study 2 found that pacing their activities and workdays with rest

worked well, and enabled them to achieve more. In the Bristol focus group, Helen spoke of how she had used training from a pacing clinic to understand how to best manage her fatigue and activity levels:

> "I was like, (enthusiastic) 'Oh, does [pacing] exist? Spoons!... 'NOW I understand! Right, okay! Ah, that's what I was doing wrong'"
>
> [Helen, Bristol focus group]

Helen's allusion to spoons is a reference to the Spoon Theory, a disability metaphor popularised online by Christine Miserandino, where she described her reduced energy levels as a result of lupus as being represented by a finite number of spoons. Those with disability or chronic illness have fewer spoons (lower energy levels), compared to the healthy population, and must recharge through rest (Haynes-Lawrence and West, 2018). The anecdotal metaphor is used to explain how many people with disability pace energy and activity, and Helen's training in pacing skills gave her the tools to understand how she was using her energy throughout the day.

Adults with JHS/EDS-HT could also learn a variety of skills to enable them to be more active participants in their own care. Transferable skills such as communication skills are valuable tools for participants to improve patient self-management, which enable effective communication when discussing or explaining their condition to others:

> "Yeah, about being able to advocate for yourself, communicate, find the right people that can help-… communicate [to] them in a way that they actually ... Understand what you're talking about, because quite often I feel like I'm, you know, Talking different languages? On a different planet"
>
> [Jody, Bristol focus group]

The majority of participants were aware of the possibility of increased symptoms during pregnancy and many were keen to share the new and unusual JHS/EDS-HT related symptoms they had experienced as a result:

> "The pregnancy, for me, like really snowballed everything, it really did."
>
> [Helen, Bristol focus group]

However, one participant during the NGT focus group was shocked to discover in light of others' stories that her JHS/EDS-HT symptoms might become more severe if she became pregnant, as her doctor had not made her aware of this information:

> "They've told me… when you're pregnant a lot of your hormones are suppressed? … I made the assumption, that maybe my hypermobility symptoms we go away? [. .] when in fact, it's the opposite… And I only learned that today? So I would rather a doctor had been able to give me that information, than me assume?"
>
> [Julie, Bristol focus group]

As with other themes, many of the issues around pregnancy also relate to a lack of reliable and good-quality information available to participants.

6.14.3 Environmental restructuring and enablement

Several participants indicated that occupational therapy input; changing their physical environment to better suit their own abilities and enable their daily living activities, had been a very effective intervention for their JHS/EDS-HT and maintaining their independence. The need to better support patients to maintain independence, rather than rely on family members or friends for physical assistance, was a key recommendation for clinicians in Study 2 (Bennett *et al.*, 2019b):

"It's just one of those small things that make such a big difference, it's not like, 'oh, okay now you got to go to physio for six months,' it's just small adjustments you can make to your life that just has such a positive [impact]."

[Alex, Bristol focus group]

However, very few had actually been offered assessment and support from occupational therapy:

"[Occupational therapy is] not something I've ever been involved in"

[May, London focus group]

"I've never had occupational therapy input!"

[Helen, Bristol focus group]

A number described having to travel to one of the two national treatment centres for JHS/EDS-HT, based in London or Stanmore, but felt that occupational therapy input and how best to modify their physical environment to better cope with their JHS/EDS-HT should be made more widely available to all patients:

"I don't think that it's (..) Fair, that there's like ... Two or three clinics in the country… that have that knowledge"

[Elsa, Bristol focus group]

Helen felt that this intervention for self-management would be very feasible to implement into the NHS, as it was readily available to other rheumatology patients:

> "[Occupational Therapy is] more effective, it would be more cost-effective as well…it's a department that exists, and other people manage to get it, so having more consistency across the NHS wouldn't be unachievable."
>
> [Helen, Bristol focus group]

Many felt that a lack of support hindered their ability to safely self-manage their condition within primary care. Some argued that this poor management had ended up costing the NHS more in the long-run, with repeated visits to accident and emergency (A&E) departments for injuries or issues that could easily have been avoided with better support to cope with their condition at home:

> "But if you took it over a period of ten years, the amount that us, as individuals… cost the NHS… because were not having the right support, so we go to A&E… I haven't had to go to A&E in the last year that I've been at [National JHS/EDS-HT treatment centre] ... And I've had the things I needed at home, to be able to deal with it."
>
> [Elsa, Bristol focus group]

By providing more efficient and direct access to emotional support and occupational therapy advice, patients with JHS/EDS-HT may be able to more effectively self-manage their condition, and cope more effectively with exacerbations in their symptoms.

6.14.4 Enablement: Access to emotional support e.g. mindfulness, counselling, CBT or books.

Chosen as one of their two preferred options by four of the nine participants, this BCT focused around increasing the means (and reducing the barriers) to accessing emotional support when self-managing JHS/EDS-HT. Kris discussed how, as she did not have a recognised mental health condition such as depression or anxiety, she was not eligible for NHS counselling, despite feeling that she could benefit from increased support:

> "That's the issue that I had with the GP, because I didn't have anything that ... they saw as being an issue? They were just like, 'so you want advice, essentially? …But, I think the benefit of [emotional support] is huge"
>
> [Kris, Bristol focus group]

As a result, a number of women had needed to pay privately for the support they needed. Participants emphasised that access to counselling services had positive effects, giving them information and encouraging them towards self-management:

> "It pushes you a bit more into that sort of ... Personal self help? , like you say going to see a psychologist, whereas this…[gives] you a load of information to use… Little things [that] might be completely unrelated [to] the condition, can have a massive positive impact on your mental well-being"
>
> [Julie, Bristol focus group]

Participants felt that this would be a feasible intervention. The group also discussed possibilities for implementation, including popular Mindfulness meditation apps, but wondered why a similar app-based self-management tool wasn't available via the NHS in order to better manage their JHS/EDS-HT:

> "So like, with the whole ... mindfulness thing… why is there not an NHS one of this? [...] Why is it someone having to pay 20 pounds a month to do this? …The NHS could do that? Not beyond the realms, is it? [. .] Accessible, by anyone, at any point"
>
> [Helen, Bristol focus group]

The inclusion of emotional support such as psychological therapies or counselling, was highlighted as a fundamental BCT for inclusion in the proposed intervention.

6.14.5 Positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped.

Many recognised the link between depression, distress and anxiety, and exacerbations of their pain symptoms:

> "And it's the emotional aspect that really ... inflames any pain that you'd feel…with anxiety, with distress, with depression (…) not- not that that causes physical symptoms, but that the things that does cause can make symptoms worse, but that's very different to it all being in your head"

[Elsa, Bristol focus group]

In a similar vein to prior discussions, participants were keen to hear examples from those with JHS/EDS-HT, who had experienced similar situations:

> **"**When you're talking to somebody who's been through it ... Their knowledge and experience sometimes seems a bit more valid then someone who's read a lot of stuff in textbooks."

[Heather, Bristol focus group]

Those with experiences of JHS/EDS-HT were seen as more understanding of the kinds of negative aspects of managing the condition, including managing the psychological impact of JHS/EDS-HT:

> "So then you start to learn, 'Okay, I need to manage my stress levels, because it impacts my health.' Or, be less anxious… you know somebody who's been through it, and can adapt how they're helping the person next to them"

[Elsa, Bristol focus group]

By providing advice and guidance from ‘similar others’ with JHS/EDS-HT, this may boost self-esteem and feelings of self-efficacy.

6.15 Discussion

This is the first study to prioritise interventions for participants to self-manage their JHS/EDS-HT using the TDF and COM-B. The overall aim of the chapter was to determine the components of a behaviour change intervention for people with JHS or EDS-HT. In order to achieve this aim we identified what would be required to change for patients to better manage JHS/EDS-HT, using the COM-B model and TDF to conduct a behavioural analysis. Next, potential intervention components were decided through extensive discussion and input by an intervention development focus group (including expert researcher and PRP input), in order to decide which behaviours identified by the COM-B mapping exercise were viable for inclusion in a self-management intervention, as recommended by Susan Michie and colleagues (Michie *et al.*, 2015). Finally, with input from key stakeholders with JHS/EDS-HT, a participant-centred modified NGT focus group method was used to identify which factors should be prioritised and participant preferences for intervention content.

Participants prioritised fourteen of the twenty-seven potential interventions with JHS/EDS-HT in a systematic modified NGT for potential implementation in primary care. The remaining interventions, while not reaching a high enough threshold for inclusion in the final list, received a wide range of scores from participants, and none was perceived as irrelevant or unrelated to their experiences of JHS/EDS-HT. The diversity of possible interventions, and participant recognition of these needs across the 27 options indicated that a holistic and multi-faceted intervention is required for participants to improve their self-management of JHS/EDS-HT.

In a recent systematic review of self-management intervention methods, a range of desired outcomes were identified, including improving participants' knowledge, skills and the use of psychosocial health interventions, such as positive social networks (Boger *et al.*, 2015). Likewise, this process indicated a range of potential intervention options, and these will now be linked to the relevant literature.

Firstly, a number of options for participant education were identified for self-management of JHS/EDS-HT. The first of these was for patients to receive education

addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures and fears about decline. In order to actively manage and take responsibility for their condition, participants need to take on knowledge and skills about how to manage their own health, especially as professional knowledge about their specific condition may be poor (Boger *et al.*, 2015, Stinson *et al.*, 2008) . Improving patients' knowledge of their condition has been used to great effect in other chronic pain self-management interventions. However, participants in a diabetes self-management education programme were keen for knowledge about their condition that they could tailor to their own circumstances, and their own personal situation (Cooper *et al.*, 2003). This idea of tailored information links with participants' newly suggested education intervention for '*tailored information when appropriate*', rather than generic information about their condition (Boger *et al.*, 2015). Recommendations for patient education in rheumatoid arthritis (based on a systematic review of the literature) also indicated the need for patient education information to be tailored to each individual patient's needs, including educational needs such as knowledge and management of their disease, knowledge of side effects and risk factors (Zangi *et al.*, 2015).

The current intervention recommendations also aimed to reduce participants' fears and catastrophising regarding their JHS/EDS-HT. Distress experienced with chronic pain, including anxiety, depression and fear of pain or injury has been shown to negatively affect participants' ability to self-manage their own condition (Devan *et al.*, 2018). Therefore, a good understanding of participants' beliefs and associated fears about their condition is a key strategy for successful self-management. Fears identified by participants in prior chapters and in the JHS/EDS-HT literature included fears relating to injuries, pain and medical treatment (Bennett *et al.*, 2019b, Berglund *et al.*, 2000, Berglund *et al.*, 2010, Schmidt *et al.*, 2015), fears of suddenly declining (Bennett *et al.*, 2019b), fears about heritability and fears relating to pregnancy and childbirth (Berglund *et al.*, 2000, Bennett *et al.*, 2019b). These beliefs were typically grounded in patients' lived experiences, or in information found on the internet (Bennett *et al.*, 2019a, Bennett *et al.*, 2019b). Interventions to manage fear have been very successful in self-management interventions for other kinds of pain. For example, self-management interventions to

manage fear-avoidance beliefs (such as catastrophising and fear of movement, (Nicholas *et al.*, 2013). The majority of self-management interventions within the literature focus on educating participants about fear-avoidance behaviours such as kinesiophobia and catastrophising in chronic pain (Nicholas *et al.*, 2013, Vowles *et al.*, 2007). Fears relating to decline in JHS/EDS-HT are associated with catastrophising; the belief that new or unusual symptoms are a signal of inevitable or impending physical decline (Bennett *et al.*, 2019b). Therefore, tailored educational information emphasising a general lack of physical decline in the majority of patients with JHS/EDS-HT would be beneficial.

Education regarding activity pacing, the monitoring of activity levels to prevent overexertion and pain exacerbations (Andersen *et al.*, 2014, Andrews *et al.*, 2015, Bair *et al.*, 2009) (Andersen *et al.*, 2014, Andrews *et al.*, 2015, Bair *et al.*, 2009 and self-help strategies for coping with flare ups in symptoms {Hainsworth, 2001 #1802, Hainsworth and Barlow, 2001) were also identified as important features by participants. A number of skills, including mastery of self-management skills, modeling behaviours and problem solving are associated with the theoretical principles of improving self-efficacy (Bandura, 1997, Hainsworth and Barlow, 2001).

In a recent systematic review of self-management interventions for people with chronic pain, practicing core self-management skills can all improve participant's acceptance of their condition (Devan *et al.*, 2018). Acceptance of JHS/EDS-HT has been identified as an important factor in successful self-management of JHS/EDS-HT (Bennett *et al.*, 2019b, Terry *et al.*, 2015) and can be a predictor of successful adjustment in chronic pain (Mccracken, 1998). Indeed, modelled behaviours, including positive behavioural modeling with similar others (those with the same or a similar condition to participants) was also found to positively promote acceptance of their condition (Willis, 2016). By observing similar peers or family members modeling behaviour, people are likely to have improved self efficacy and confidence in their ability to master a skill (Willis, 2016).

Participants also indicated preferred options for training, including skills development focusing on self-advocacy, assertiveness and communication. Research on doctor-patient communication has indicated that by providing patients with the opportunity to communicate, patients can be empowered to manage their own

health and chronic conditions, thereby promoting and improving self-efficacy (Allen *et al.*, 2008). An exploration of a humanisation approach to managing JHS/EDS-HT recommended giving patients the agency to manage their own condition, such as through self-referral to physiotherapy (Clark and Knight, 2017). In addition, by recognising emotions such as fear, healthcare professionals can gain patients' trust and understanding, enabling those with JHS/EDS-HT to communicate their needs (Clark and Knight, 2017). A recent qualitative systematic review and meta-synthesis of self-management interventions identified a need for better communication across all stakeholders (patients, healthcare professionals, family and friends) in order to positively support patient self-efficacy and self-management of chronic pain (Devan *et al.*, 2018).

Likewise, assertiveness training, while not as prominent a feature as others in behaviour-change and self-management interventions, was also raised by participants in the Study 2 interviews as a key facilitator to successfully self-manage their JHS/EDS-HT. Those who had attended hospital pain management courses spoke of how they now had the assertiveness to advocate for what they needed.

Self-advocacy has been an important element raised by others with chronic pain. In an exploration of identity in women living with chronic pain in Canada, many cited learning to advocate for themselves as an essential step in adjusting to their condition. This included advocating for their needs at work, asking for assistive devices in public, and advocating for their own treatment and care within the medical system. Once women in the study began to advocate for their needs, and receive support and validation from others, their perceived control over the condition, and level of confidence increased (Sharpe *et al.*, 2013).

Participants' combined voting and NGT results identified two interventions that related to environmental restructuring and enablement, and these related to the physical and psychosocial impact of JHS/EDS-HT. Firstly participants were keen for self-management supported by occupational therapy input, in order to adjust their environment to complete tasks independently from their family members. The key barrier in this case was participants' lacking the physical capability to manage their own activities, and instead relying upon family members or partners for assistance. However, as seen in the Study 1 systematic review and Study 2 thematic

analysis, depending on others for support with daily activities caused feelings of guilt and shame (Bennett *et al.*, 2019a, Schmidt *et al.*, 2015).

Occupational therapy input has successfully been used to influence the self-management of other chronic pain conditions, including fibromyalgia (Nielson and Jensen, 2004). Although not a typical self-management programme, Lewin and colleagues (2013) evaluated the impact of a multidisciplinary rehabilitation intervention, incorporating task modification, assistive technology, injury prevention and chronic disease self-management, which showed improved independence in activities of daily living, compared to a control group receiving usual services (Lewin *et al.*, 2013). For post-stroke patients, a fall-risk self-management intervention combining group yoga and occupational therapy were used to address a number of risk factors for falls, including balance self-efficacy, fear of falling, concern about falling relating to basic and more demanding activities (physical and social) and management of fall risk factors (Atler *et al.*, 2017, Schmidt *et al.*, 2015). This included performing activities differently or modifying the environment around them with the aim of improving safety, including adding more light, removing trip hazards and adding grip to surfaces. Modifying activities included planning ahead and completing activities with more awareness, and learning how to assist themselves to get up off the floor, rather than asking others for help (Atler *et al.*, 2017). Although the environmental modifications to prevent injuries in JHS/EDS-HT would be slightly different (with a focus on planning movement and avoiding injury), participants with EDS-HT have been reported as likely to fall due to joint instability (Rombaut *et al.*, 2011a). Indeed, as many as 96% of of those with EDS-HT surveyed had experienced a fall within the previous 12 months, with 68% reporting balance problems such as unsteadiness and stumbling when walking (Rombaut *et al.*, 2011a). Participants in the stroke OT intervention cited improved confidence in their ability to manage their own condition, and greater optimism regarding their own physical abilities (Atler *et al.*, 2017). Learning how to make adaptations to one's own environment can enhance feelings of independence and provide a sense of successful adjustment (Kubina *et al.*, 2013). Therefore, incorporation of occupational therapy into a self-management strategy for managing JHS/EDS-HT could be beneficial, in terms of

improving participants' confidence. This support could potentially reduce incidence of accidental injuries and participants' associated fear of movement.

Lastly, many were keen for an intervention to feature enablement, in order to access emotional support such as mindfulness, counselling, CBT or books. Enablement can be defined as increasing means or reducing barriers to increased capability or opportunity (Michie *et al.*, 2013). The principles of CBT have been used as the foundation of a number of empirically supported self-management interventions for the management of chronic pain. For example, Bourgault and colleagues (2015) self-management intervention utilised CBT skills, in addition to exercise and relaxation techniques for patients with Fibromyalgia-related chronic pain (Bourgault *et al.*, 2015). In recent promising recommendations for managing rheumatoid arthritis, the need for patient education to include discussion of emotional issues, psychological support, and support from healthcare professionals in managing emotional distress has been highlighted (Zangi *et al.*, 2015). Predominantly using methods such as mindfulness, breathing exercises, and stress-management skills, the main aims of emotional support programmes have been to promote acceptance, enhance wellbeing and alleviate emotional distress by imparting participants with the skills to manage positive and negative emotions (Zangi *et al.*, 2015).

6.15.1 Strengths and limitations

This study has a number of strengths. Firstly, the COM-B and TDF models have a strong theoretical underpinning and have facilitated the development of recommendations for a self-management intervention for patients with JHS/EDS-HT, through targeting a number of behavioural barriers to self-management. Using this method, it was possible to identify a number of influences on participants' behaviour that would have been difficult to identify using quantitative methods. For example, prior research had identified participants with JHS as being significantly more fearful than the general population but with this qualitative approach a number of specific fears in relation to automatic motivation and knowledge about JHS/EDS-HT have been identified; from fears about potential injury (Lumley *et al.*, 1994, Schmidt *et al.*,

2015, Terry *et al.*, 2015) to fears about future deterioration of their condition leading to catastrophising about symptoms (Bennett *et al.*, 2019b).

A second strength was the involvement of stakeholders at every stage of the process. Involvement of participants likely to receive the end-stage intervention is important when developing, evaluating and implementing complex interventions (Nilsen *et al.*, 2006). Participants with JHS/EDS-HT were involved, both at the identification stages (PRP Sue Harris), and at the NGT stage, which also encouraged discussion and debate regarding their individual views of each proposed intervention. Consultation with patients is likely to result in material that is more relevant, understandable and readable to patients (Nilsen *et al.*, 2006). Indeed, there was evidence during the NGT discussions that participants found materials to be very relevant to their lived experiences, and were freely able to alter the wording of their proposed interventions to improve understanding and coherence.

The use of a modified NGT and focus group methodology enabled group consensus to be established regarding preferred items for a JHS/EDS-HT self-management intervention. The methodology enabled useful quantitative and qualitative data regarding participants' use, experiences, and preferences. However, it is acknowledged that by utilising patient focus groups, thorough exploration of certain sensitive issues (such as sexual dysfunction) were less likely to be voiced by participants in this method than in an interview setting.

One limitation is the smaller number of participants in this study. In the Study 2 telephone interviews, participants were selected purposively to maximise diversity in relation to age, gender, ethnicity and location to ensure a wide-ranging variety of participant opinions and experiences (Bennett *et al.*, 2019b). Participants in the NGT study were not as diverse a group in comparison. One reason for this may be the face-to-face nature of this methodology. Feedback from participants who were unable to attend the London focus group indicated that the significant effort required to travel and attend the group in person, may have been a barrier to those who wanted to take part, particularly if they had more severe chronic pain or disability. Although the modified NGT process enabled priorities to be identified, this was based on the opinion of 9 women, and therefore may not be as representative

of the priorities that others may choose, such as men or women from more diverse communities and ethnic backgrounds.

Despite attempts made to contact participants in the Bristol focus group, few participants chose to vote on items from the London focus group. This was considered several weeks after the completion of data collection for both groups, therefore future use of this method may have greater success by allocating time for follow-up voting with each group as quickly as possible after additional focus groups have taken place.

In addition, participants' additional ideas for intervention options had to be matched to the COM-B and TDF definitions by the group facilitators (SB & SP) at the time of the NGT focus group. While every effort was made to ensure that these definitions both reflected what participants wished to see in the proposed intervention, and that these were true to other interventions proposed by the method, the fact that these additional ideas could not be given the same time and consideration as the other twenty proposed interventions is a potential limitation. However, in consultation, refinement and discussion of key concepts with participants at each of the modified NGT focus groups, participants were content that the additional ideas proposed reflected what they would like from a self-management intervention.

Although the Behaviour Change Wheel was a very thorough and structured process, there were some limitations regarding the usability of the method. As the BCW was developed to be applicable to a wide range of behaviour change interventions, it has resulted in quite general definitions. Only one example of behaviour was given for each definition by the authors, and the researcher found, during the mapping process, that barriers could be mapped to more than one BCW category. In cases such as these, there was no guidance regarding which to choose, so independent judgement had to be made in response to relevant literature. In addition, a list of potential intervention functions would be indicated for each COM-B and TDF factors, and again, it was for the researcher to judge, with input from the study PRP, which of these would be a best fit for 'solving' the barrier identified. Although extensive supervision, collaboration and discussion with other researchers with expertise in this area was sought by the researcher, the lack of guidance and

potential for subjectivity bias in such a structured process was a concern. Having such a complicated and definition-heavy process proved quite difficult to explain to lay participants with no prior experience of this method. To mitigate this methodological weakness, the researcher provided all BCW and intervention-related definitions in hard copy, and was very careful to verbally define each word and ensure participant understanding at every stage of voting and discussion.

6.16 Conclusions

In summary, this final stage of the research provided a valuable insight into what patients with JHS/EDS-HT like to see in a self-management intervention. It also gave important patient perspectives regarding the appropriateness, feasibility, acceptability, barriers and facilitators to preferred content for the intervention.

While original plans to involve healthcare professionals were not fully realised at this stage due to time and recruitment constraints, there is still scope for future research to involve a number of professionals from a variety of sources and gain feedback regarding the acceptability and feasibility of the intervention in the context of NHS resources. This information will be vital in informing future research and development of a holistic, patient-centred intervention for the management of JHS/EDS-HT.

7 Chapter 7: Discussion

7.1 Introduction

Chapters 4, 5 and 6 presented and discussed the individual findings at each stage of this thesis. This chapter combines and discusses these findings in respect to the wider JHS/EDS-HT literature, considers strengths and weaknesses of the overall research programme, the implications that these findings have for future JHS/EDS-HT research and final conclusions. The purpose of these sections is to is to expand upon the results identified in an effort to provide a further understanding of the psychosocial impact of JHS/EDS-HT on adults, and to present ideas for future research, as recommended and indicated by the results of these studies. Finally, a concluding section is presented to evaluate what has been achieved with this research.

7.2 Summary of the research programme

7.2.1 Thesis aims

The overarching aims of this thesis were:

- To understand the lived experiences of people with JHS and EDS.
- To explore the psychosocial, cognitive and behavioural impact of JHS/EDS-HT.
- To determine recommendations for the components of a self-management behaviour change intervention for people with JHS/EDS-HT.

These aims were addressed through a sequential multiphase mixed methods design: a systematic review and thematic synthesis of qualitative literature (Study 1, Chapter 4); seventeen qualitative semi-structured interviews analysed using thematic analysis (Study 2, Chapter 5); and two modified nominal group technique consensus exercises (Study 3, Chapter 6).

7.2.2 Study 1: To understand the lived experiences of people with JHS and EDS (Chapter 4).

The aim of this first study was to understand the lived experiences of people with JHS and EDS. This was achieved with a systematic review and thematic synthesis of qualitative literature examining the lived experiences of adults with JHS and EDS (Bennett *et al.*, 2019a). This is the first qualitative systematic literature review to examine and appraise the JHS and EDS literature. Focusing on, and consolidating findings from qualitative studies of participants lived experiences; this review identified a broad range of common findings identified across the included papers.

The results of Study 1 indicated that JHS and EDS had a significant emotional and physical impact. A lack of awareness and understanding of JHS/EDS led to long waits for a diagnosis and questions regarding the legitimacy of their symptoms (Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016, Palmer *et al.*, 2016b). Participants described distressing experiences where they had been aware of pain with local anaesthetic (Berglund *et al.*, 2000). Some hid their JHS/EDS-HT in an effort to be treated like everyone else (Schmidt *et al.*, 2015, Terry *et al.*, 2015). To complete daily tasks, others relied on help and support from friends or family but this brought guilt, depression and frustration (De Baets *et al.*, 2017, Berglund *et al.*, 2000). A fear of injury led to some participants being less sociable than they would like, which could cause anxiety (Schmidt *et al.*, 2015). Some were also fearful of pregnancy complications, or of their children inheriting JHS/EDS-HT from them (Berglund *et al.*, 2000). Treatment, advice and holistic, hands-on input from a physiotherapist with knowledge of JHS and EDS was described as extremely helpful. Participants also recognised the limits of physiotherapy, due to the underlying collagen defects in JHS and EDS (Palmer *et al.*, 2016b, Simmonds *et al.*, 2017). Participants described 'redefining' their own version of 'normal', as they would have JHS and EDS for life (De Baets *et al.*, 2017, Palmer *et al.*, 2016b), including breaking activities down into smaller steps, and thinking of different ways to manage life's challenges (Schmidt *et al.*, 2015).

The results identified in this review provided original insight into the lived experience of adults with JHS and EDS, including participants' fears and anxieties, limitations to their daily activities, a lack of recognition of the condition, and the need for multidisciplinary care. However, these results were limited, and there was scope to better understand how

participants coped with their JHS or EDS, as other means of self-management, such use of information or social support received little mention in this synthesis of the literature.

7.2.3 Study 2: To explore the psychosocial, cognitive and behavioural impact of JHS/EDS-HT (Chapter 5).

In order to achieve the aim of Study 2, there were two objectives. The first of these was to identify the psychosocial impact of JHS/EDS-HT by examining participants' lived experiences. Participants in this study were recruited from a local NHS Trust, and via social media advertisements with Ehlers-Danlos Support UK (EDS-UK). Some were also members of The Hypermobility Syndromes Association (HMSA). Prospective participants were screened for inclusion in the study using the Hakim and Grahame (2003) Five-point questionnaire for GJH and the Hospital Anxiety and Depression Scale (HADS, (Zigmond and Snaith, 1983). Participants were purposively selected for inclusion using a sampling frame detailing; age, gender, ethnicity, degree of GJH and levels of anxiety and depression. Results from semi-structured telephone interviews indicated a substantial psychosocial impact of JHS/EDS-HT, including limitations to mobility due to symptoms of pain, injury, or digestive, or urinary issues, restrictions to work and education, elements of social stigma and a lack of understanding of JHS/EDS-HT when seeking healthcare (Bennett *et al.*, 2019b).

The second objective of Study 2 was to understand how participants cope with their JHS/EDS-HT. Participants identified a number of ways of coping. Psychosocial and cognitive appraisals included acceptance of the permanent, lifelong nature of their condition, and the physical limitations accompanying this, including staying positive in the face of injuries or pain, and a sense of determination to complete the tasks that they set their minds to. Social support from others with disabilities, as well as gaining knowledge about JHS/EDS-HT gave participants the confidence and assertiveness to explain their needs and limitations to others.

Physical and behavioural coping included participants modifying their interests, exercises and activities, to better accommodate weakness or dislocating joints, which led to improved physical fitness and psychological wellbeing. Participants praised physiotherapists with specialist knowledge of JHS/EDS-HT, many of whom had given them tactics and

techniques to manage dislocations, in addition to emotional support encouraging a more positive, optimistic outlook.

7.2.4 Study 3: To determine the components of a behaviour change intervention for people with JHS/EDS-HT (Chapter 6)

The results from Studies 1 and 2 were then mapped to behaviour change theory, The Theoretical Domains Framework and COM-B model, in order to identify barriers to self-management of JHS/EDS-HT (Michie *et al.*, 2015). The results of this mapping indicated a number of potential behaviour change interventions, which were presented to a new cohort of participants in two modified NGT focus groups. Participants were then asked to identify and quantitatively rank which two behaviour change interventions were most important to them, and the appropriateness, acceptability, feasibility, perceived barriers and solutions of their preferred intervention options. From these combined qualitative and quantitative findings, potential interventions to support participants with JHS/EDS-HT were identified.

7.3 Original contributions to knowledge

The multiphase study described above has provided the following contributions to knowledge. These recommendations have been developed, based on key findings identified at each stage of the research, and how they could relate to the participant-identified behaviour change intervention priorities identified in Chapter 6. The results indicate the need to understand participants' perspectives and lived experiences before attempting to offer potential intervention options. New and original findings and associated recommendations from this thesis are discussed below, with recommendations for future interventions.

7.3.1 The psychosocial, cognitive and behavioural impact of JHS/EDS-HT is substantial, and there is a lack of support available to patients nationally. (Study 1, Study 2, Study 3)

Participants identified a need for greater psychological support to help manage aspects of the psychosocial impact of JHS/EDS-HT that they found difficult to control, such as sexual dysfunction, depression, distress, frustration and feelings of loss. In relation to the wider

literature, patients with JHS suffered significantly greater psychological distress compared to those without the condition, namely depression, panic disorders (Smith *et al.*, 2014b) and anxiety (Sanches *et al.*, 2012). The multi-systemic impact of JHS and EDS has been shown to lead to restricted physical and psychological functioning and poor health-related quality of life (Berglund and Nordstrom, 2001, Maeland *et al.*, 2011). Given the lack of recognition and reliable information available to participants about JHS/EDS-HT, as indicated in Studies 1, 2 and 3 it is understandable that patients may experience negative psychological consequences as a result. For example, Rhiannon wondered in Study 2 "*"Is my body going to completely fall apart?",* and Roger echoed the fear that *"one day I might not be able to do anything".*

Participants in the Study 3 NGT focus groups indicated that emotional support should be available as soon as possible following diagnosis of JHS/EDS-HT in order to better support participants' emotional needs. Participants in Study 2 and 3 emphasised that access to counselling and emotional support services had a positive impact on their ability to manage their condition, giving them information and encouraging them to use a variety of coping strategies. These results are very similar to those of a multicentre survey for psychological support in inflammatory arthritis (IA; (Dures *et al.*, 2016). Like JHS/EDS-HT, patients with IA have around twice the prevalence of anxiety and clinical depression compared to the general population (Geenen *et al.*, 2012). While demand for psychological support was also high, fewer than a quarter of patients had been asked about social or emotional issues, yet 46% of those surveyed would like to discuss the psychological impact of their condition, including support managing pain and fatigue (82%), their emotions (57%), their work and leisure activities (52%), relationships (37%) and depression (34%,(Dures *et al.*, 2016).

For the JHS/EDS-HT patient population, multidisciplinary interventions such as cognitive behavioural therapy in combination with a tailored exercise programme showed improved performance in daily activities, improved muscle strength and endurance, and decreased kinesiophobia, as measured by the Tampa scale for kinesiophobia, and is the first intervention to show an improvement in kinesiophobia for the JHS/EDS-HT population (Bathen *et al.*, 2013). It is recognised that JHS/EDS-HT is a complex condition with significant psychosocial impact. Therefore, it is recommended that emotional support materials are

developed for participants with JHS/EDS-HT, and that participants are offered emotional support such as mindfulness, counselling or CBT for patients, from diagnosis onwards.

As suggested by the mapping process in Study 3, the use of first-person modeling narratives could be used to better support participants in the self-management of their condition. Although the terminology 'first person modeling' is a phrase unique to the BCW, patient education using first-person peer support has been successfully employed in self-management education for African-American women with lupus (Faith *et al.*, 2018, Williams *et al.*, 2017). Patient education that incorporated peer support from others with the same condition has been shown to demonstrate improvements in measures of self-efficacy, health distress and depression (Faith *et al.*, 2018, Williams *et al.*, 2017). Therefore, a further recommendation is in relation to patient education, for positive first-person modeling narratives that address some of the negative aspects of JHS/EDS-HT and how they coped.

A further behaviour change intervention identified by participants included patient education regarding how to navigate social support, from external sources such as the local council, government benefits, Access to Work or Disabled Students' Allowance (DSA). By proving support to continue working or studying, participants with JHS/EDS-HT can be better supported to improve their lives for the better. However, how best to navigate the sometimes complex world of disability reforms was highlighted, therefore the need for better support and information in this area in the form of patient education is recommended.

7.3.2 2. A lack of good quality, reliable, tailored information for patients with JHS/EDS-HT (Study 2, Study 3).

The scarcity of information and accurate, reliable information for patients about JHS/EDS-HT resulted in some participants becoming very afraid regarding how their condition was going to affect them in the future (Study 2). Because of this lack of reliable information, participants described using a combination of self-sourced information from books and the Internet and social comparisons to others with the condition. However, if these social comparisons were made to people whose JHS/EDS-HT symptoms had greatly disrupted their lives, participants could become very fearful. Many described how this would lead to feelings of anxiety and panic when faced with new symptoms, concerned that this was the

sign that their JHS/EDS-HT was causing their body to decline. This finding was a surprise to the researcher, given that all participants were recruited from JHS/EDS-HT support groups, and would therefore have access to more information than the majority of patients. However, as number of participants in the NGT focus groups in Study 3 indicated, the information offered to them at diagnosis had been out-dated and too focused on arthritis. Indeed, research has indicated that individuals may not put as much trust in information found online, if they are unable to appraise the information for reliability, and they can experience difficulties with the sheer volume of online health information (Lee *et al.*, 2014).

Of possible interventions to manage this, participants in Study 3 favoured guidance and education regarding how to evaluate the information they discovered about JHS/EDS-HT, and which sources of information they could trust when looking up information about their condition. Participants also advocated for the use of a combination of education to address their knowledge of JHS/EDS-HT, and the provision of tailored, accurate information at diagnosis. Therefore, it is recommended that guidance is developed for patients regarding trusted, accurate sources of information for JHS/EDS-HT.

In order to counteract these fears, in addition to more accurate information, participants suggested the idea of examples of model behaviour from a mentor who also has JHS/EDS-HT. Having a mentor or positive role model could give participants the opportunity for positive social comparison, as interaction with other patients has been shown to help reduce fear relating to symptoms, providing example behaviours for people to aspire to or imitate (Grahn and Danielson, 1996, Krouse, 2001, Michie *et al.*, 2011). Parents with JHS/EDS-HT in Study 1 spoke positively of becoming motivational role models; encouraging their children to adopt positive behaviours in managing their JHS/EDS-HT (De Baets *et al.*, 2017). This pattern of mentoring behaviour has also been observed in online chronic illness communities, such as “veterans” sharing their experiences (both their successes and failures with self management behaviour strategies), which enabled other members experiencing similar symptoms to vicariously learn which strategies were the most beneficial to others in similar situations (Willis, 2016, Willis and Royne, 2017). This study provides credibility to the notion that internet-based support groups could facilitate members’ self-efficacy to practice chronic pain self-management behaviours (Willis, 2016). Therefore, it is recommended that educational education for patients addressing knowledge

and management of JHS/EDS-HT, pain control, self-help measures and fears about decline, delivered by a mentor with JHS/EDS-HT.

7.3.3 Patients who are able to pace their activities are better able to manage their daily activities and work commitments (Study 1, Study 2, Study 3).

Education regarding activity pacing, the managing and awareness of activity levels to prevent overexertion and pain exacerbations, was positively appraised by participants in Study 3 (Andersen *et al.*, 2014, Andrews *et al.*, 2015, Bair *et al.*, 2009) and self-help strategies for coping with flare ups in symptoms (Hainsworth and Barlow, 2001) were also identified as important features. Fear of potential physical injury and having increased pain can lead to people with EDS-HT deliberately avoiding conceivably high-risk activities such as sports and regular exercise (Rombaut *et al.*, 2010). Indeed, the systematic review of the literature in Study 1 indicated that injury fears prevented participants from being as socially active as they would like, *"I'm in a constant state of anxiety, waiting for the next injury and trying to pre-empt anything that's going to cause it"* (Terry *et al.*, 2015).

Supporting participants with JHS/EDS-HT to manage their symptoms and activity levels using pacing skills builds on recommendations of other researchers in this area. For example, Baeza-Velasco *et al.,* (2019) recommended therapeutic strategies, including activity pacing, for management programmes for EDS-HT patients presenting with kinesiophobia (Baeza-Velasco *et al.*, 2019). Participants in Study 2 described how pacing their workweek enabled them to work without needing to recover from fatigue.

As participants in Study 3 also indicated that they would welcome training in pacing skills, it is recommended that education materials are developed regarding the consequences of overexertion and how to cope with pain exacerbations, in order to achieve participation in daily activities. Others with JHS/EDS-HT could give educational examples of behaviours, for patients to aspire to or imitate.

Widespread pain in JHS/EDS-HT may be due to centralised sensitisation to pain in patients with JHS/EDS-HT (Rombaut *et al.*, 2015, Scheper *et al.*, 2017). In response, a combination of mastery of self-management skills, modeling behaviours and problem solving have been associated with the theoretical principles of improving self-efficacy (Bandura, 1997, Hainsworth and Barlow, 2001) and would be a beneficial intervention option in this patient group. This would give participants the option to model group

behaviours, problem solve, help others and relate to peers who have experienced similar circumstances.

7.3.4 Difficulties with sexual relationships due to vaginal or bladder prolapse in women, or erectile dysfunction in men (Study 2).

Difficulties with sexual relationships due to vaginal, rectal or bladder prolapse in women, or erectile dysfunction in men are a significantly under-researched finding. In a recent study of autonomic dysfunction symptoms associated with JHS/EDS-HT, most of the men involved in the study did not want to complete the erectile dysfunction symptom profile, so its impact was not recorded (De Wandele *et al.*, 2014).

Participants in Study 2 feared a negative impact on their relationships and, due to the underlying cause of JHS/EDS-HT being a defect in collagen, were unsure of what treatments would be available to support them. While some attention has been given to women with JHS/EDS-HT who experience pain during sexual intercourse caused by vaginal dryness (Castori, 2012) little consideration has been given to the impact of prolapse (Norton *et al.*, 1995) or erectile dysfunction on sexual functioning within the JHS/EDS-HT literature.

These results indicate a further recommendation for improved information, support and recognition of potential intimacy issues in JHS/EDS-HT, particularly for health professionals in primary care, as problems with sexual functioning may markedly influence the patient's quality of life.

7.3.5 Women with JHS/EDS-HT were fearful of passing on their genes to their children, of their increased likelihood of injury during pregnancy, and were concerned that they would not be able to look after their children due to JHS/EDS-HT symptoms.

7.3.6 There is a lack of information and support for patients with JHS/EDS-HT during pregnancy, when JHS/EDS-HT related symptoms in a number of patients are likely to increase. (Study 1, Study 2, Study 3)

This thesis contributes to the small body of previous literature that explores participants' lived experiences of pregnancy and becoming a mother (Berglund *et al.*, 2000, De Baets *et*

al., 2017). Pregnancy complications in the EDS-HT literature are mixed; from women who have experienced very few complications (Castori, 2012) to other studies that have reported increased instances of pelvic pain (Volkov *et al.*, 2007) premature rupture of membranes and preterm delivery (Lind and Wallenburg, 2002). Participants with JHS/EDS-HT are also likely to have increased symptoms during pregnancy, such as worsening joint laxity and pelvic pain, thought to be due to the hormone relaxin (Marnach *et al.*, 2003), and a number of participants in all stages of this research confirmed these flares in symptoms during pregnancy. Fears and anxiety around pregnancy complications and becoming a mother were common to all stages of this research, and the wider JHS/EDS-HT literature (Berglund *et al.*, 2000, De Baets *et al.*, 2017). However, others cited that, while a difficult choice, gaining a concrete diagnosis had helped them to make an informed decision about whether or not to have children (De Bates *et al.,* 2017, Study 1).

It was a revelation to the researcher to hear the widespread nature of some women's symptoms during pregnancy, such as swallowing difficulties and multiple dislocations, and the strategies participants had employed to try to adapt, such as sleeping in leg braces in an effort to avoid dislocations (Study 2). As with previous research, women were anxious regarding the possibility of their child inheriting JHS/EDS-HT from them, and this was cited as an important consideration for a number of participants. Although using slightly different terminology, the pregnancy literature indicates that role models can provide positive, natural and healthy examples of pregnancy and birth to expectant mothers (Budin, 2011). Realistic and attainable role models have also been linked with important stages of identity transition, from existing identity to maternal identity during pregnancy (Hennekam, 2016).

During Study 3, the need for improved education, training and information for participants regarding what to expect was well-received by participants. Therefore, it is recommended that templates outlining potential increased JHS/EDS-HT symptoms during pregnancy, and what to do, are developed to act as a useful tool to support pregnant women. In addition, modeling of coping strategies from mothers who had successfully had children was chosen, in order for participants to have positive role models for managing any increases in their JHS/EDS-HT symptoms. Therefore, it is recommended that education, training and information is developed, covering what to expect during pregnancy with JHS/EDS-HT.

7.3.7 A need for occupational therapy support for participants with JHS/EDS-HT in order to maximise independence in everyday activities and reduce feelings of guilt and shame (Study 1, 2 and 3).

At times, participants in all studies were reliant on help from their partners, friends, or family, to complete daily tasks that they were not able to do themselves, either because of symptoms such as fatigue or pain, or because of risk of injury (Berglund *et al.*, 2000, De Baets *et al.*, 2017). However, participants felt embarrassed, ashamed, and that they were failing in their roles by not being able to complete these tasks independently (Bennett *et al.*, 2019b, Schmidt *et al.*, 2015). In order to overcome this barrier, the Study 3 intervention category '*environmental restructuring and enablement*' was employed, and participants' physical environment would be altered (with input from an occupational therapist), in order for participants to better achieve daily tasks and goals independently.

However, participants in Study 3 indicated that, unlike other rheumatic diseases, where occupational support is provided as standard; very few participants had received input from an occupational therapist. Many felt that having to travel to distant national specialist treatment centres for JHS/EDS-HT was too geographically restrictive, and felt that advice about how to modify their physical environment in order to better self manage their JHS/EDS-HT should be more widely available. Elsa implied that without effective aids and support at home, participants were more likely to cost the NHS more in the long term, due to more frequent injuries and dislocations. Improved support for participants with JHS/EDS-HT has the potential to improve independence and confidence, particularly in relation to personal care, washing and dressing. This is a key indication for future research that rehabilitation and support for people with JHS/EDS-HT needs to take into account strategies for maximising independence in activities of daily living. Therefore, it is recommended that support materials emphasising the benefits of occupational therapy are developed, to assist healthcare professionals and patients.

7.3.8 A need for improved recognition and awareness of JHS/EDS-HT in primary care, including issues with local anaesthetics.(Study 1, 2 and 3)

Although highlighted as an important issue in prior research, the lack of awareness and recognition of JHS/EDS-HT within the medical community was in line with other examples within the literature. Participants in all stages of this study also experienced very long delays in receiving an accurate diagnosis, and a lack of understanding and knowledge of the condition from healthcare professionals. There is a need for increased awareness of associated issues between with local anaesthetics and JHS/EDS-HT (Berglund *et al.*, 2000). A number of participants in Study 2 recounted significant pain from reduced effectiveness of local anaesthetics, thought to be due to the underlying collagen defect in JHS/EDS-HT, and a lack of awareness of this potential problem from GPs and healthcare professionals (Bennett *et al.*, 2019b, Wiesmann *et al.*, 2014). These negative experiences could lead to a fear of treatment, which may prevent those with JHS/EDS-HT from seeking appropriate medical care (Berglund *et al.*, 2000). Therefore, it is recommended that future research focus on interventions to support improved training and awareness of JHS/EDS-HT for healthcare professionals.

Participants across all sections of the thesis indicated a lack of understanding from others about their JHS/EDS-HT. Some hid their JHS/EDS-HT from others in order to appear 'normal' (Bennett *et al.*, 2019b, Schmidt *et al.*, 2015, Terry *et al.*, 2015). Sometimes, participants' restricted mobility resulted in frustration, as they could not manage to do as much as their friends. Prior research has indicated that better communication across stakeholders can improve patients' self-efficacy and self-management of chronic pain (Devan *et al.*, 2018, Williams *et al.*, 2017). In addition, research from other conditions such as the Arthritis Self-Management Programme (ASMP) aims to enhance participant sense of confidence in their ability to use appropriate self-management skills to meet the needs. Topics in the ASMP include cognitive symptoms management and guidance on how to communicate with healthcare professionals and set goals. Participants who learned to advocate for their needs received better support and validation from others, improved perceived control over their condition, and increased levels of confidence (Sharpe *et al.*, 2013). Therefore, it is recommended that training is developed and offered to participants focusing on advocacy, assertiveness and communication, in order to be able to communicate their needs to other people effectively.

7.3.9 The lived experiences and impact of JHS/EDS-HT on men, including differences in coping styles (Study 2).

This thesis has improved understanding of men's experiences of JHS/EDS-HT, compared to women. While only a small number of men participated, the qualitative results in Study 2 indicated that the body changes caused by JHS/EDS-HT such as reduced strength and frequent injury caused threats to participants' sense of masculinity.

This goes against Western body ideals, which indicate that masculinity requires strength, not showing pain, to never appear to be weak to others and be self-sufficient (Gibbs, 2005). The symptoms and experiences of men with JHS/EDS-HT, with potential easy bruising and injury, chronic pain or difficulty standing, needing to ask others for help with activities or having to ask for a seat on a train may undermine men's independence and sense of self (Gibbs, 2005). The intervention suggested that perceived threats to participants' social role and identity could be mitigated by participant education to manage their beliefs and perceptions about body image. Although not researched in JHS/EDS-HT, exploration of men's psychosocial experiences of RA have also found this to be threatening to their sense of power and control over their own lives (Flurey *et al.*, 2018). However, as in Study 2, where men with JHS/EDS-HT bonded and shared social and emotional support over video games, men also used their problem-solving strategies to better cope with their RA (Bennett *et al.*, 2019b, Lack *et al.*, 2011).

7.4 Strengths and limitations of the thesis

7.4.1 Sampling

Seventeen participants were interviewed for Study 2, and nine participants took part in face-to-face NGT focus groups in Study 3. Participants in Study 2 were purposively sampled using a sampling frame based on criteria relevant to JHS and EDS-HT research. These included age, gender, ethnicity, GJH and levels of anxiety and depression. One advantage of conducting research with a purposive sample of participants from a variety of socioeconomic, educational and geographical backgrounds could have the benefit of improving the generalisability of this research to a UK population.

Interviewing participants with a broad range of experiences within the phenomenon being studied has been identified as important within the qualitative literature (Greenhalgh, 2019). Given their diverse geographical locations, participants had a range of experiences of JHS/EDS-HT, and a wide variance in accessibility to treatment, with those nearer to London more able to access specialised care, compare to those in more isolated areas, or from low socioeconomic backgrounds. This pattern has also been noted in access to specialised treatment for patients with breast cancer (Gentil *et al.*, 2012). Those in more geographically isolated areas spoke of a greater reliance on the internet for information and social support, rather than face-to-face support. However, participants in the NGT focus groups in Study 3 were not as diverse a group in comparison, and this was hypothesised as being due to the face-to-face nature of this methodology. Future research with this population may benefit from consideration of remote participation, such as the internet-based recruitment and telephone interview methods employed in Study 2.

Another consideration is transferability, which refers to the degree to which qualitative results can be generalised or transferred to other contexts, people, or settings. With transferability, it cannot be assumed that the things learned in one context cannot easily be applied in another (Morgan, 2007). As Tracy and Hinrichs (2017) argue, traditionally quantitative concepts of generalisability are not helpful in the context of qualitative research, as statistical generalisations are drawn from randomized, representative samples. In this example, data is isolated from context or situations, whereas in qualitative research, results are typically in-depth and culturally situated (Tracy and Hinrichs, 2017). The authors argue that transferability, or the analysis of contexts and embodied experiences can be achieved, in order that readers may appreciate the findings, and ultimately apply, or 'transfer' these to their own situations and experiences (Tracy and Hinrichs, 2017). Readers of the research must decide if the setting and results of the study are similar enough to resonate with their own lived experiences (Kuper *et al.*, 2008). In the present thesis, it was hoped that, rather than relying on traditional ideas of generalisability, participants would be able to 'transfer', or reflect upon their own experiences of living with JHS/EDS-HT. In addition, as recommended by Kuper and colleagues (2008), efforts were made to draw parallels between the results of the present study, and links to the relevant literature, both for JHS/EDS-HT and for other chronic pain conditions, such as lupus or RA. Finally, feedback

was sought from Sue, the study PRP, regarding whether results at each stage were comparable to her own experiences as a patient with JHS/EDS-HT.

A further limitation is the 'dual role' of the candidate as a researcher, and as a patient. This presented potential limitations in terms of subjectivity, bias, over-identification or under-identification with participants. These risks were addressed by ensuring strict quality assurance measures during data collection and analysis.

In Study 3, the intervention development team was broadened to include additional researchers with valuable independent external expertise in qualitative (Jen Pearson) and behaviour change research (Laura Swaithes), in addition to the study patient research partner (Sue Harris), who were actively involved in identifying and re-wording relevant behaviour change techniques. These changes reduced the risk of subjectivity or one-sidedness in the analysis and presentation of the results.

In Study 2, the risk of bias was addressed by having a random selection of interview transcripts checked against the original recordings by the research team (NW, TM, SP), thereby allowing those not directly involved in data collection to audit the results, reducing bias and ensuring accuracy (Malterud, 2001). The research team (NW, TM, SP) also reviewed the findings and themes identified in the results, using a process of peer debriefing, which allowed for critical reflection on the judgements and themes identified within the data, in order to prevent over- or under-identification with participants. The quality of the Study 2 results was independently assessed using the consolidated criteria for reporting qualitative research (COREQ) framework; a 32-item assessment for reporting interviews and focus groups (Tong *et al.*, 2007) by the candidate and director of studies (Professor Shea Palmer). When Study 3 coding was complete, it was refined, reviewed and approved by two researchers with expert experience in using each method of behaviour change: the COM-B (Professor Nicola Walsh) and TDF (Dr Jen Pearson). By incorporating external expertise and input at each stage of the collection, analysis and interpretation of the data, the use of externality helped to bring more objectivity to the process, and reduce the risk of biased conclusions, or results based on the candidate's own experiences as a patient. Although

involving participants with the condition under study as partners in the research process is considered a methodological strength, recognising the limitations to Sue's input is an important consideration.

European League Against Rheumatism (EULAR) guidelines for the involvement of patients in research have noted that 'the patient perspective' does not truly exist, and patients own experiences of their conditions and what they have learned from others can be very different from what other patients may go through (Caeyers and De Wit, 2013). In addition, the views of a single partner cannot represent all patients with the same diagnosis. While opinions, experiences and feedback from Sue as the study PRP were very helpful to the researcher within each stage of the research process, the limitations of these experiences as being from only one patient are noted as a potential limitation. In future studies, employing a pair of research partners or a small team of research partners may reduce this bias and provide scope for a more diverse range of inputs. For example, in the development of the Psoriatic Arthritis Impact of Disease (PsAID) score, multiple forms of PRP input and participation were used throughout development of the patient outcome measure, including the identification of life impact domains, providing impact on wording or offering alternative terms (Kirwan *et al.*, 2017). This was particularly important in relation to the psychosocial impact of PsA, where participants preferred the inclusion of questions that asked about embarrassment, shame, social participation and depression, which healthcare professionals had not considered as important priorities (Kirwan *et al.*, 2017).

A further limitation is that all participants in the study had a self-reported diagnosis of JHS or EDS-HT. In the UK, a rheumatologist gives a diagnosis of Hypermobility Spectrum Disorder (HSD) and Hypermobile Ehlers-Danlos Syndrome (hEDS) using the latest 2017 criteria (Malfait *et al.*, 2017), after a clinical assessment of the patients presenting symptoms. Without the ability to assess participants in a face-to-face consultation with a rheumatologist, this research instead used the Five Part Questionnaire (5PQ, Hakim & Grahame, 2003) to screen for clinically significant joint hypermobility. However, reliance on self-reported information may have resulted in participants giving a 'false positive' diagnosis, which risks participants without JHS/EDS-HT participating in the study. Certainly, in studies of rheumatoid arthritis (RA) and ankylosing spondylitis (AS), self-reported

diagnosis were found to have low accuracy when checked against medical records (Videm *et al.*, 2017). Of 2703 participants with a self-confirmed diagnosis of RA, only 19.1% of those with self-reported RA and 15.8% of those with AS were proven by medical records to be accurate diagnosis (Videm *et al.*, 2017). Participants may have given a false-positive diagnosis of JHS or EDS-HT for a number of reasons, such as those in whom a diagnosis of JHS/EDS-HT had been suspected by a physiotherapist or GP, and who were waiting for a referral to rheumatology. Alternatively, those with suspected JHS/EDS-HT may have later been assessed and found not to meet the diagnostic criteria, or be more likely to have GJL. In addition, some may have used the internet and information provided by support groups or social media to make a self-diagnosis. This limitation is an important consideration, and future studies would benefit from the use of in-person clinical assessment to screen hEDS and HSD from false self-report. A further option in categorising diagnosis in patients is the use of diagnostic codes, however these rely heavily on the consistency and quality of patient notes and reporting, and changes in diagnostic nomenclature over time in EDS, can make this an unreliable source. For example, a recent case-control comparison of the diagnosed prevalence of EDS and JHS in Wales identified participants using diagnostic codes (Demmler *et al.*, 2019). The JHS/EDS cohort was identified using either GP diagnostic codes of EDS or JHS within primary care GP data, or International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnostic terms within secondary care data (hospital admissions), between 1st July 1990 and 30th June 2017. However, even with diagnostic codes, there were still limitations in the identification of patients with JHS and different EDS subtypes. Due to changes in nomenclature in 1997, not all EDS subtypes used prior to 1997 (Type III, Type IV) were included within the GP diagnostic code data. In addition, the majority of patients (86%) had been coded within GP data as 'EDS' without a specified subtype, with only 12% coded as hypermobile EDS (Demmler *et al.*, 2019). Limitations to the diagnostic accuracy of the data resulted in all EDS subtypes being combined during analysis, however the authors noted that they were unable to comment on the reliability of the diagnostic codes or diagnosis within the primary care dataset (Demmler *et al.*, 2019).

7.4.2 Study 2: Screening of participants for clinically significant anxiety and depression:

Although a requirement of the NHS Ethics Committee in the process of approval for Study 2, the lack of recruitment of participants with clinically severe anxiety or depression may be a limitation of the present study, as these are the patients most likely to require interventions and support. As a result, these findings may not be as relevant to participants with JHS/EDS-HT who have severe anxiety or depression. Indeed, depression and anxiety have been shown to prospectively predict levels of pain and pain-related disability in patients with chronic pain (Lerman *et al.*, 2015). However, the candidate acknowledged that participants with severe anxiety or depression may have difficulty conveying their thoughts by phone or, based on email feedback from prospective participants, may have found the idea of a phone interview too overwhelming. Future studies wishing to examine participants' experiences and coping with JHS/EDS-HT alongside severe anxiety or depression may wish to explore other means of participant interaction that respondents would find less stressful, such as qualitative data collection using free-text surveys, or via email, with options for participants to convey their thoughts and experiences without the worry of having to interact with a stranger.

7.4.3 Involvement of patients, PRP and reflexivity

Great care was taken during the planning, data collection and analysis of each stage of this study to ensure that the results and avenues for research identified were as representative of adult men's and women's experiences of JHS/EDS-HT as they could be. While the methods put in place to aid reflexivity have been covered in Chapters 3 and 5, external input from Sue as the PRP was sought in relation to design and wording of study materials, and the representativeness of the findings. Independent opinion from the supervisory team (Study 1 and 2) and external researchers with BCW expertise (Study 3) was sought at each stage of data collection, data mapping and analysis. It is also worth noting that, in addition to the study PRP (SH) agreeing with the findings as an accurate representation of her experiences with JHS, during the Study 3 NGT focus groups, participants also expressed that they could fully identify with the findings of Study 1 and 2, on which recommendations for interventions were based; "*You've just described my whole life!*" [Kelly, Bristol Focus Group].

However, there are some limitations to these provisions: the opinions of Sue as PRP are only representative of one person's experience, and these opinions may therefore not be representative to all adults with JHS/EDS-HT.

7.5 Indications for future research

7.5.1 Determining recommendations for a self-management intervention to manage JHS and EDS-HT: Input from a representative sample of healthcare professionals.

At present, there is no pathway of care for patients presenting with JHS/EDS-HT symptoms in primary care, aside from referral to physiotherapy. Participants have told us that psychological support for their condition is wanting, and several studies have indicated a lack of trustworthy information about JHS/EDS-HT leading to emotional responses such as fear and catastrophising. A further phase of this research could involve asking other relevant stakeholders (healthcare professionals with experience of JHS/EDS-HT) for their views on the self-management intervention options, and whether these would be feasible and achievable in primary care, using focus groups or individual interviews. Input from healthcare professionals using the BCW methodology has been successfully used to develop a number of interventions, including interviews with audiologists (n=10) to improve hearing aid use in adults (Barker *et al.*, 2016), in semi-structured interviews with GPs in the development of an intervention to improve immunoglobin requests in primary care (Cadogan *et al.*, 2016), and, nurses, doctors and pharmacists in the exploration of antibiotic prescribing in primary care (Fleming *et al.*, 2014) These focus groups or interviews can provide useful data regarding social and contextual factors relating to the barriers identified, and give practical, targeted intervention functions to target these (Fleming *et al.*, 2014). Therefore, the views and opinions of healthcare professionals most likely to provide support to adults with JHS/EDS-HT would be very valuable in the further development of a self-management intervention.

7.5.2 Pilot study of a self-management intervention for adults with JHS/EDS-HT.

As a result of data and feedback from healthcare professionals outlined above, the intervention could be further developed with input from patients and representatives from JHS/EDS-HT charities and clinicians, using a co-creation process. A future pilot study testing a supportive self-management intervention for adults with JHS/EDS-HT could then be targeted. As a result it is anticipated that patients could potentially benefit from improved quality of life and social outcomes and have the potential to be more confident in managing their JHS/EDS-HT and decreasing use of healthcare resources.

Based on the results of the potential behaviour change interventions, a number of outcome measures could be used to examine patient outcomes. Outcome measures are used to assess the consequences of health management interventions on disease, and can be divided into objective (observer-dependant) measures, and subjective (observer-independent or self-rated) measures (Bijlsma, 2004).

In the present study, the prioritised elements of a proposed self-management intervention have indicated that any measures used would have to cover a wide range of patient-reported outcomes. Outcome measures could be measured at baseline, and at 3 and 6 months post-intervention, in order to identify any change as a result of the self-management intervention. However, the current evidence base for OT and physiotherapy input is still limited, with little research exploring clinical outcomes for positioning, posture management and patient education in JHS/EDS-HT (Smith *et al.*, 2014a). As discussed by Engelbert and colleagues (2017) there is a need for further research to identify and validate suitable outcome measures in children and adults with JHS/EDS-HT. Possible outcome measures include:

Activities of daily living: The Canadian Occupational Performance Measure (COPM): In a multidisciplinary rehabilitation programme (Bathen *et al.*, 2013) limitations to performing activities of daily living were assessed with the COPM (Carswell *et al.*, 2004), with participants invited to define their self-assessed occupational performance problems in areas of self-care, productivity and leisure in a semi-structured interview and quantitative Likert scales. The scale measures any change in participants self-perception of their performance in occupational activities over time. Importantly for patients with JHS, this measure includes self-care, leisure activities and productivity, all important psychosocial factors raised by participants with JHS/EDS-HT (Bennett *et al.*, 2019b).

Anxiety and depression: The Hospital Anxiety and Depression Scale (HADS, (Zigmond and Snaith, 1983), as used as a screening tool in Study 2, would be an effective measure of anxiety and depression in this population, without the risk of false-positive overlap scores for symptoms of chronic illness, such as pain or fatigue.

Fear: Although no JHS/EDS-HT specific measure has been developed, prior studies have used the Fear Survey Schedule (FSS-III) with participants who have JHS/EDS-HT to assess a range of common fears and phobias (Bulbena *et al.*, 2006, Pailhez *et al.*, 2011). A more pain-specific measure is the Fear Assessment in Inflammatory Rheumatic Diseases (FAIR) questionnaire (Gossec *et al.*, 2018). Developed to measure fear and psychological distress in patients with RA and axial spondyloarthritis (axSpA), patients beliefs about the nature of their disease may be wide-ranging and fearful, leading to restricted behaviours and psychological distress (Gossec *et al.*, 2018). The outcome measure could potentially be adapted to evaluate fears in patients with JHS/EDS-HT, in order to closely examine fears relating to their condition before and after an intervention.

JHS/EDS-HT specific measures of physical functioning, emotional functioning and fatigue: The Bristol Impact of Hypermobility (BIoH) questionnaire is a condition-specific outcome measure designed to assess the impact of JHS/EDS-HT (Palmer *et*

al., 2017). Due to significant links between JHS/EDS-HT and fatigue (Terry *et al.*, 2015, Palmer *et al.*, 2017) the BIoH also includes the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales (BRAF-NRS), with questions relating to fatigue severity, effect of fatigue and coping. The scale has been validated and been shown to be able to accurately distinguish between those with and without JHS as well as strong concurrent validity and test-retest reliability (Palmer *et al.*, 2020, Palmer *et al.*, 2017).

Kinesiophobia: The Tampa Scale for Kinesiophobia to assess pain-related fear of movement. Multidisciplinary interventions for JHS/EDS-HT including a combination of cognitive behavioural therapy and a tailored exercise programme showed improved performance in daily activities, improved muscle strength and endurance, and decreased kinesiophobia (Bathen *et al.*, 2013).

Pain: the Visual Analogue Scale (VAS) is a simple but effective measure of pain intensity, and used with JHS/EDS-HT populations in prior studies to assess pain intensity (Booshanam *et al.*, 2011, Zhou *et al.*, 2018, Rombaut *et al.*, 2011b).

Self-efficacy: As so many elements of the prioritised behaviour change interventions feature structured education and training, a measure of self-efficacy, and any changes before and after any intervention. The Chronic Disease Self-Efficacy Scale was developed to asses the effectiveness of the Stanford Chronic Disease Self-Management Programme, and consists of three self-efficacy beliefs; to perform specified behaviours, to manage their condition and to achieve certain outcomes, on a total of 10 subscales (Brady, 2011). Some items also assess confidence in obtaining results, such as getting information about their condition, communicating with doctors, self-efficacy to manage their condition in general, and self-efficacy relating to social and leisure activities (Brady, 2011). Many of these items are similar to those mentioned by participants in earlier stages of the research as things that they found difficult to manage with JHS/EDS-HT, therefore evaluating whether there had been any change in participant self-efficacy before and after the self-management intervention would be beneficial.

7.5.3 Development of patient education guides and materials

Participants in all studies indicated a lack of reliable up-to-date patient information available to adults with JHS/EDS-HT. They described the current provision of arthritis-focused leaflets from the NHS as quite poor, focused on older men and women, and out-dated. Particularly in Study 3 many felt that the patient education information that they had been provided with was not relevant or appropriate to them as young women. In order to effectively manage their condition, participants need reliable and up-to-date knowledge about their condition and its treatment, in order to maintain optimum psychosocial functioning (Clark *et al.*, 1991). Future work in the area of JHS/EDS-HT self-management could potentially work in collaboration with patient support groups such as the HMSA and EDS-UK in order to develop patient-designed, patient-focused educational information that supports their need for information from diagnosis onwards.

7.5.4 The lived experiences of minority groups in JHS/EDS-HT

Although only a small number of men (n=4) participated in Study 2, their sharing gave new insight into men's experiences with JHS/EDS-HT, the effect of the condition on their masculinity, and the coping styles that they employ. In addition, despite recruiting using a sampling frame and interviewing participants of mixed ethnicity, the views and experiences of participants from black and minority ethnic communities are under-represented within all JHS/EDS-HT research, despite GJH affecting people of black and Asian ethnicity to a greater extent. Although purposive sampling was employed in Study 2 to gain a broad representation of participants from those available, further work is still required to assess whether any new themes would be identified with greater representation of participants from black and minority ethnic populations, or from men's experiences, whose views in JHS/EDS research have yet to be explored in depth.

7.5.5 Pregnancy and JHS/EDS-HT

These findings have indicated a lack of information for mothers with JHS/EDS-HT regarding pregnancy, building on beliefs highlighted in prior research about participants' perceived consequences of having children (Berglund *et al.*, 2000, De Baets *et al.*, 2017). It is vital that prospective parents with JHS/EDS-HT are provided with information regarding motherhood, before, during and after their pregnancy. Numerous authors have cited the importance of providing both practical and psychosocial information for all mothers, in order to convey realistic expectations (Currie, 2009) and improve adjustment to parenthood and becoming a mother (Darvill *et al.*, 2010). Valuable guidelines have been published for midwives in the management of women with JHS/EDS-HT, before, during and after pregnancy, which also account for potential pregnancy-related complications as a result of collagen laxity, including increases in pelvic girdle pain and instability (Pezaro *et al.*, 2018). Work exploring the experiences of women with JHS/EDS-HT in relation to pregnancy, childbearing, and their experiences of maternity care and provision of information would be very helpful, perhaps using internet-based surveys to ensure ease of participation.

7.5.6 Impact on family members

Participants in each study routinely acknowledged the impact that having JHS/EDS-HT had on their family, including feelings of shame and guilt that they could not always fulfil their obligations as parents, husbands, or wives due to the symptoms of JHS/EDS-HT. Although the impact of chronic pain conditions such as rheumatoid arthritis have been considered on partners (Matheson *et al.*, 2010) the impact and involvement of family members of those with JHS/EDS-HT have been neglected in current research. Qualitative studies exploring these experiences, perhaps with recommendations for family support and consideration of the heritable nature of JHS/EDS-HT would be a further valuable area of exploration.

7.5.7 Lack of awareness of JHS/EDS-HT

Although not explored in great depth in this thesis, these results contribute to the growing body of evidence within the literature of a lack of knowledge of JHS/EDS-HT within primary and secondary care professionals (Berglund *et al.*, 2010, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016a). It is therefore recommended that healthcare professionals receive greater training and support, in order to improve awareness and recognition of JHS/EDS-HT.

7.6 Conclusion

The findings of this study have provided a novel insight into men's and women's experiences of JHS/EDS-HT and the associated psychosocial impact. While participants have proposed and approved a range of behaviour change interventions for the effective self-management of JHS/EDS-HT, results indicate that patients with JHS/EDS-HT carry a significant psychosocial burden.

Study 1 drew together a range of qualitative findings relating to the lived experience of JHS/EDS across the literature, in the first thematic synthesis in this area. The findings indicated a lack of awareness and understanding of JHS/EDS-HT from friends, family, healthcare professionals and the general public, leading to very long waits for diagnosis, often of many years. Participants were not keen to disclose their JHS/EDS-HT to others, but often relied on help from friends and family to complete daily tasks and activities, which led to frustration and guilt. Treatment and input from physiotherapists was fundamental in the management of their condition.

Study 2 comprehensively detailed adult men's and women's experiences of JHS/EDS-HT and provided a novel understanding of how psychosocial factors, including family relationships, work colleagues, social networks and attitudes and enthusiasm of healthcare professionals all play important roles in shaping men's and women's experiences of JHS/EDS-HT. Novel findings have been identified, including a need for further information about JHS/EDS-HT, participants' fears regarding new symptoms and potential declines in ability, and a desire for greater independence in daily activities. Several coping approaches were identified by participants, including building social networks, finding out more about JHS/EDS-HT online, adapting their

activities to better manage the impact of the condition and a need to educate healthcare professionals involved in their care.

Study 3 indicated participants' desire for more dependable information, support from similar others with JHS/EDS-HT such as mentors, and a dearth of dependable psychological support to manage the psychological and emotional impact of the condition. Participants were keen for patient education to better manage and pace their activities, and flares in pain or symptoms, navigating benefits, evaluating information on the internet and improved training and support for mothers with JHS/EDS-HT when pregnant. In addition, input from professionals to restructure and better enable activities was noted, in order to improve independence and reduce reliance on family members.

Further research to support participants has been identified, including qualitative input from a representative sample of healthcare professionals, development of potential interventions to improve information provision and address psychological support, and increased awareness of JHS/EDS-HT.
As a result of these findings, a number of recommendations for future work are indicated:

Recommendation 1: It is recommended that future research and support recognises the need for patient advice and rehabilitation to improve and maintain independence in activities of daily living. Participants in Study 1 and 2 who had help from family members to complete activities described feelings of guilt and shame. This advice could be a specialised occupational therapist or physiotherapist and adaptations made to the environment to boost patients' confidence in the ability to manage their own condition independently.

Recommendation 2: A number of participants spoke of difficulties with sexual relationships due to prolapse or erectile dysfunction, and associated anxieties. This has indicated a need for improved awareness of these issues within primary care. It is recommended that future work in this area explore these under-researched findings and, with patient input, advice and support materials for patients affected by these issues could be developed.

Recommendation 3: The provision of reliable information and materials is vital, both for healthcare professionals and patients, to reduce misinformation, anxiety and fear. Participants in Study 3 indicated that they did not feel represented by the limited information available to them, and therefore the need for patient involvement as collaborative partners in the design and production of these materials would be of utmost importance. It is therefore recommended that future research be conducted to improve provision of information resources for patients with JHS/EDS-HT.

These research findings provide a new insight into the psychosocial impact of JHS/EDS-HT. Through future work improving people's knowledge and skills, we can aim to give patients with JHS/EDS-HT the best possible support in the self-management of their condition:

> "You don't give up, and you keep going back, and you keep trying, and trying to get somebody that will help you… Because if I hadn't have kept trying I would never have known that I had EDS, I would never have got the help and support I have done, and whilst now it seems dried up, at least I've gained a lot of valuable knowledge…and I know now what exercises work for me, and don't work for me, so I would say take back your power, learn as much as you can about the condition, because knowledge can have power, and that is your strength."
>
> [Lauren, Interview 006]

Appendix A: Illustrative quotes from the five main themes in Study 1 and their underlying subthemes.

Theme and subthemes	Illustrative quotes	References containing relevant data
Lack of professional understanding		
Negative attitudes of healthcare professionals:	"The doctor asked him if the injuries were caused by child abuse, since our daughter had large bruises on her arms and legs. We were worried and didn't know her injuries were caused by EDS" (Berglund *et al.*, 2000) "I made an appointment to see a highly recommended surgeon about my ankle degeneration...I was told to remove my shoes and slacks, and to wait for the doctor. When he arrived, he brought with him (without asking me) a medical student . . . Without even asking me what my problem was, he began to forcefully sublux my knees, ankles, and fingers, to demonstrate the 'flexibility' of someone with EDS to the medical student. The entire time, he was looking at her, not me, and speaking to her, not me" (Berglund *et al.*, 2010) I hate getting that vibe from people…I'm the last person who would want to make this up! (Bovet *et al.*, 2016) "My experience is that the PTs [Physical Therapists] just don't know about [EDS]." (Bovet *et al.*, 2016) "When I went and had my knee operation, they just said 'Oh, you're hypermobile'. That's it. 'This is why we're putting you in a brace.' That's it." (Palmer *et al.*, 2016a)	(Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Simmonds *et al.*, 2017, Palmer *et al.*, 2016a)
Long journey to diagnosis:	"It takes so many years to get diagnosed" (Palmer *et al.*, 2016b) "I just needed to see somebody who knew what we were dealing with. I didn't want to be the educator." (Bovet *et al.*, 2016) "I went to see a doctor (orthopaedic) relating to pain in the hands and the knees and he basically told me that it was all psychosomatic and that I was also bulimic. I left the office in a rage and still in pain." (Berglund *et al.*, 2010) "It was not until some years later that we met a doctor who knew that it was EDS and explained it to us." (Berglund *et al.*, 2000) "The diagnosis became clear through self-examination. Finding the last missing piece of the puzzle is indescribable; recognizing yourself and saying 'Eureka!', finally finding out what you were looking for all along (De Baets *et al.*, 2017)	(Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016, De Baets *et al.*, 2017, Palmer *et al.*, 2016b)
Fear of treatment:	"I had a sprained ankle and when the nurse was going to cut the bandage open with the scissors, I asked her to be careful since my skin is very fragile. I guess she thought I was fussy, so she ended up cutting my skin and I had to have sutures. I guess that's the kind of stuff that makes me not trusting them." (Berglund *et al.*, 2000) "To get stitches is horrible when they do not know how to take care of me." (Berglund *et al.*, 2000) "I hesitate about returning for any medical needs even when urgent care may be required. I'm on strike. Only if my life is at risk will I return." (Berglund *et al.*, 2010)	(Berglund *et al.*, 2000, Berglund *et al.*, 2010, Bovet *et al.*, 2016)
Theme and subthemes	Illustrative Quotes	References containing relevant data
Social stigma		

Negative attitudes of others:	"I don't want to knock myself out and spend two days in bed and have the children come in and see me and go away thinking 'that mum's really ill.'" (Schmidt *et al.*, 2015)	(De Baets *et al.*, 2017, Berglund *et al.*, 2000, Schmidt *et al.*, 2015, Terry *et al.*, 2015)
Hiding JHS/EDS from others to appear 'normal':	"I never showed my legs, I always had stitches and bruises all over, always wore long pants, no shorts during school gym. My brothers and sisters and I would try to hide all the bruises and scars. In the summer everyone else was tanned while we had white scars all over." (Berglund *et al.*, 2000)	(Terry *et al.*, 2015, Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015)
Negative attitudes towards self:	"It makes you feel really guilty and it makes you feel like you have let people down and it makes you feel like you constantly let people down." (Schmidt *et al.*, 2015) "When I was at school I just had to sit at the side while they were doing all the games, they sort of almost, I felt they were blaming it on me." (Terry *et al.*, 2015)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Palmer *et al.*, 2016b, Schmidt *et al.*, 2015)

Theme and subthemes	Illustrative Quotes	References containing relevant data
Restricted life		
Fear of future injury:	"It's just difficult to know how much to push yourself because then you are worried about injuring and then you're setting your- self back, it's a vicious cycle really" [28]	(Berglund *et al.*, 2000, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016a)
	"It's on your mind the whole time because I'm constantly thinking about where my hands and feet are" (Terry *et al.*, 2015)	
	"I just avoided, avoided exercise I suppose, and avoided, sort of, exacerbating it" (Palmer *et al.*, 2016a)	
Limited social participation:	"I wanted to study to become a dietician but when I found out that I needed six months practice in catering - which is impossible to manage - I was terribly disappointed. I had to change my career plans." (Berglund *et al.*, 2000)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016a)
	"I feel that [JHS/EDS-HT] limits me in the exercise that I want to do because I've always been a very sporty person" (Palmer *et al.*, 2016a)	
Fluctuating nature of JHS/EDS:	"My legs hurt and then it fades away. Two hours later my shoulder is aching and then it starts inside my knee" (Berglund *et al.*, 2000)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016b, Palmer *et al.*, 2016a)
	"The days that I feel fairly well I keep busy furnishing miniature cabinets and when I feel like today, I might get ideas through books or museums. The days when I am really bad I can just think about what I would like to do." (Berglund *et al.*, 2000)	
	"One day you can be very indisposed and the next day you can jump over small houses" (Berglund *et al.*, 2000)	
	"For example, walking is one of the things I like to do. But this is not always possible; it depends on my pain. If it is not possible, it is not. But these are things that make me feel really happy. If I'm able to manage that little walk, I'm happy. If I can manage a larger walk… but if it is not going to happen then I'm happy with the little ones… and those are things I love to do." (De Baets *et al.*, 2017)	
	"I had been going to the gym for a while, you know, under the probably mistaken belief that […] lots of heavy lifting would sort of, you know, strengthen the muscles and therefore the tendons and then it would improve the situation, although actually it had been making it worse, I think" (Palmer *et al.*, 2016a)	

Theme and subthemes	Illustrative Quotes	References containing relevant data
Trying to "keep up"		
Depending on others:	"Something that is potentially high risk of dislocation then it's just not worth doing it, because then you got to take someone's time getting you to the hospital, so they've got to stop doing what they want to be doing, you got to waste someone's time the next day looking after me and the baby.	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*,

	It's just not worth it, so you just don't do it." (Schmidt *et al.*, 2015)	2016b)
	"I like to be able to be in control of what I do. It's important to me. I don't want to knock myself out and spend two days in bed and have the children come in and see me and go away thinking that mum's really ill" (Schmidt *et al.*, 2015) "I am awfully tired, more than what's normal and I have to watch out so I don't get hurt, which happens because I'm not careful" (Berglund *et al.*, 2000)	
Sex, pregnancy and heritability:	"Now that I have children, I have become more confident…I would never want to go back to the period before I had children… Never! They give meaning to my life and structure to your day…You have less time to think, EDS-HT has become something secondary, not a main thing on my mind… which is actually logical." (De Baets *et al.*, 2017)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017)

Theme and subthemes	Illustrative Quotes	References containing relevant data
Gaining control		
Negotiating physiotherapy:	"The whole medical system is set up so that it was focused on my feet. But now my PT recognizes to work on the whole body, not just my feet." (Bovet *et al.*, 2016)	(Bovet *et al.*, 2016, De Baets *et al.*, 2017, Palmer *et al.*, 2016b, Simmonds *et al.*, 2017, Terry *et al.*, 2015, Palmer *et al.*, 2016a)
	"Because of, I think, the way – at least in my experience – that the NHS seems to approach things, they have a sort of, 'you're here for one joint' approach, which is quite difficult, because you go: 'Well, I'm floopy all over,'. And then you have to have the conversation about 'Well, which is the most difficult?' You're like 'Well, it's kind of all related', so if, like, if my knee is stronger and I'm doing less weird things with my knee, then my hip will feel better because - and I can say that, and to me it's obvious, that if you fix - just because it's your hip that hurts it doesn't mean that it is actually the problem. It could well be that your knee is the issue, making you do weird things with your hip, but there's this, 'This is the joint, and we will deal with this joint,' when that isn't really" (Palmer *et al.*, 2016b)	
	"Then, as you say, being given some more exercises that weren't helpful because they did seem to cause more pain which then sets you back even more and then you seem to get into the cycle of never sort of making any progress and then the treatment's over because you only get a few sessions" (Palmer *et al.*, 2016b)	
	"So could they not do a package where you actually went back every six months to see somebody regardless of how you were feeling?" (Palmer *et al.*, 2016b)	
	"I found heavily guided exercise the most beneficial; I think that I am less likely to have an awareness of how well I am completing the set tasks than "normal" people. My last physio saw me for far longer than usual and also booked me follow up appointments monthly after each course finished so she could keep checking my effectiveness of repetition afterwards, this enabled me to have plenty of feedback to keep my energy from being wasted by mis-performing exercises." (Simmonds *et al.*, 2017)	
	"I'm not a normal person, I don't have the joints of a normal person, so that isn't actually relevant to me" (Palmer *et al.*, 2016a)	
Helping their children:	"I need to think about how I can help my children so they don't end up with choosing the wrong occupation or hurting themselves too much" (Berglund *et al.*, 2000)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Palmer *et al.*, 2016a)
	"You know what kind of pain your children will suffer, and you know they can't escape it" (De Baets *et al.*, 2017)	
	"I think it's very important that we, as mothers, because we experience it ourselves, give our children a positive image. Two things are important in the children's education: their education in general, but also education in how they can live with their illness" (De Baets *et al.*, 2017)	
	"You wake up and just 'oh please not today, I really can't face it' but you haven't got a choice you've just gotta get going, especially when you've got kids and things, it's-you've just got to keep going" (Palmer *et al.*, 2016a)	

Redefining normality:	"You can measure it [i.e. the success of physiotherapy] by parts of [the] body I guess because I, although I don't feel remotely better in many parts I still say that my last physiotherapy was a success because it significantly helped me with my shoulders so that I, I like suffer a lot less pain in that area of the body now, so I call it a success but when you get to my knees and ankles and neck and back it did [not] do that much, the neck surgery was a success because that significantly reduced the neck pain although I still get probably more muscular now than any joints but that's still again one part of it, so there's lots of other areas that are still very bad, so erm I guess that in order to say that I'm better every bit would have to have improved significantly to say that they didn't affect my day to day life, but to have individual parts improve is still a success." (Palmer *et al.*, 2016b) "Because I kind of understand and have an interest in it, I think it makes it really easy and go really quick so I suppose it's where someone who doesn't really know about it, they've got to learn about it first because you can't tell someone to do it if they don't understand it." (Palmer *et al.*, 2016b) "You won't be fine, not completely." (Palmer *et al.*, 2016b) "I teach like rock-climbing, surfing, body boarding and all of that stuff, like, and I'm not going to stop doing it because I'm in pain like you can't live your whole life with pain dictating what you can and can't do." (Terry *et al.*, 2015)	(Berglund *et al.*, 2000, De Baets *et al.*, 2017, Schmidt *et al.*, 2015, Terry *et al.*, 2015, Palmer *et al.*, 2016b)

Appendix B: Ethical approval of Study 2 from the UWE Faculty Research Degrees Committee (FRDC)

Faculty of Health &
Applied Sciences
[redacted]

Our ref: JW/lt

Miss Sarah Bennett
[redacted]

Dear Sarah

Application number: HAS.16.06.161

Application title: Understanding and Managing the Psychological Impact of Joint Hypermobility Syndrome

NHS Application Number: 16/LO/0511

Your NHS Ethics application and approval conditions have been considered by the Faculty Research Ethics Committee on behalf of the University. It has been given ethical approval to proceed with the following conditions:

You comply with the conditions of the NHS Ethics approval.
You notify the Faculty Research Ethics Committee of any further correspondence with the NHS Ethics Committee.
You must notify the Faculty Research Ethics Committee in advance if you wish to make any significant amendments to the original application.
If you have to terminate your research before completion, please inform the Faculty Research Ethics Committee within 14 days, indicating the reasons.
Please notify the Faculty Research Ethics Committee if there are any serious events or developments in the research that have an ethical dimension.

Any changes to the study protocol, which have an ethical dimension, will need to be approved by the Faculty Research Ethics Committee. You should send details of any such amendments to the committee with an explanation of the reason for the proposed changes. Any changes approved by an external research ethics committee must also be communicated to the relevant UWE committee.
Please note that any information sheets and consent forms should have the UWE logo. Further guidance is available on the web:
http://www1.uwe.ac.uk/aboutus/departmentsandservices/professionalservices/marketingandcommunications/resources.aspx
Please note that the University Research Ethics Committee (UREC) is required to monitor and audit the ethical conduct of research involving human participants, data and tissue conducted by academic staff, students and researchers. Your project may be selected for audit from the research projects submitted to and approved by the UREC and its committees.

Please note that your study should not commence at any NHS site until you have obtained final management approval from the R&D department for the relevant NHS care organisation. A copy of the approval letter(s) must be forwarded to Leigh Taylor in line with Research Governance requirements.

We wish you well with your research.

Yours sincerely

Dr Julie Woodley

Chair

Faculty Research Ethics Committee

c.c. *Shea Palmer*

Appendix C: Ethical approval of Study 2 from the NHS Health Research Authority (HRA).

NHS
Health Research Authority
London - West London & GTAC Research Ethics Committee
Nottingham REC Centre
The Old Chapel
Royal Standard Place
NG1 6FS

18 April 2016

Miss Sarah Bennett
[redacted]

Dear Miss Bennett

Study title:	**Understanding and Managing the Psychological Impact of Joint Hypermobility Syndrome**
REC reference:	**16/LO/0511**
IRAS project ID:	**174518**

Thank you for your letter of 15th April 2016, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Assistant Tadeusz Jones, NRESCommittee.London-WestLondon@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Contract/Study Agreement [Study Agreement - UWE Offer Letter]	1	17 August 2014
Copies of advertisement materials for research participants [Email Advert V1 29-02-16]	1	29 February 2016
Copies of advertisement materials for research participants [Poster Advert V1 07-03-16]	1	07 March 2016
Covering letter on headed paper [Response to REC]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Indemnity Letters UWE UMAL 15-16]	1	01 January 2016
GP/consultant information sheets or letters [HMSA Supporting Letter to Physios V2 09-02-16]	2	09 February 2016
Interview schedules or topic guides for participants [Interview Topic Guide V1 08-03-16]	1	08 March 2016
IRAS Application Form [IRAS_Form_04032016]		04 March 2016
IRAS Application Form XML file [IRAS_Form_04032016]		04 March 2016
IRAS Checklist XML [Checklist_04032016]		04 March 2016
IRAS Checklist XML [Checklist_08032016]		08 March 2016
Letters of invitation to participant [Participant Invitation Letter Phase 1 V1 29-02-16]	1	29 February 2016
Letters of invitation to participant [Participant Invitation Letter Phase 2 V1 29-02-16]	1	29 February 2016
Other [Tim Moss CV V1 07-03-16]	1	07 March 2016
Other [Nicola Walsh CV V1 07-03-16]	1	07 March 2016
Other [Indemnity Letters UWE UMAL EL PL 15-16 V1 08-03-16]	1	08 March 2016
Other [Indemnity Letters UWE UMAL PI 15-16 V1 08-03-16]	1	08 March 2016
Other [Distress protocol]	1	04 April 2016
Other [Risk assessment form]	1	14 April 2016
Other [Participant reply slip]	2	31 March 2016
Other [Screening questionnaires]	2	07 April 2016
Participant consent form [Consent Form V1 07-03-16]	1	07 March 2016
Participant information sheet (PIS) [Participant Info Sheet Phase 2 Questionnaires V1 07-03-16 PDF]	1	07 March 2016
Participant information sheet (PIS) [Participant Information Sheet Phase 2 Control V1 07-03-16]	1	07 March 2016
Participant information sheet (PIS)	2	15 April 2016
Research protocol or project proposal [Understanding and Managing the Psychological Impact of Joint Hypermobility Syndrome Protocol V1 29-02-16]	1	29 February 2016
Summary CV for Chief Investigator (CI) [Sarah Bennett Summary CV V1 11-02-16]	1	11 February 2016
Summary CV for student [Sarah Bennett Research CV V1 11-02-16]	1	11 February 2016
Summary CV for supervisor (student research) [Shea Palmer CV V1	1	07 March 2016

07-03-16]		
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Study Flow Chart V1 18-02-16]	1	18 February 2016
Validated questionnaire [Screening Questionnaires V1 29-02-16]	1	29 February 2016

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

16/LO/0511	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

Dr Elizabeth Lund
Chair

APPENDIX C2: Study 2 Research and Development Access: North Bristol NHS Trust

Letter of Access 1

North Bristol NHS
NHS Trust

[redacted]

13 June 2016

Private and Confidential

Miss Sarah Bennett
[redacted]

Dear Miss Bennett

Letter of access for research

Title of Study: Understanding and Managing the Psychological Impact of Joint Hypermobility
Study Number: 3733

This letter confirms your right of access to conduct research through North Bristol NHS Trust for the purpose and on the terms and conditions set out below. The right of access commences on 15 June 2016 and ends on 1 March 2017 unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from North Bristol NHS Trust (R & D approval). Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from the Trust's R & D office giving permission to commence the project.

The information supplied about your role in research at North Bristol NHS Trust has been reviewed and you do not require an honorary research contract with this NHS organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out.

You are considered to be a legal visitor to North Bristol NHS Trust premises. You are not entitled to any form of payment or access to other benefits provided by us to employees and this letter does not give rise to any other relationship between you and North Bristol NHS Trust, in particular that of an employee.

While undertaking research through North Bristol NHS Trust, you will remain accountable to your employer but you are required to follow the reasonable instructions of your nominated research manager in the Trust or those given on her/his behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by this NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with North Bristol NHS Trust policies and procedures, which are available to you upon request, and the Research Governance Framework. You are required to co-operate with North Bristol NHS Trust in discharging its duties under the Health and Safety at Work Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on North Bristol NHS Trust premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of a contract holder and you must act appropriately, responsibly and professionally at all times.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (http://www.dh.gov.uk/assetRoot/04/06/92/54/04069254.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged; I enclose a form in order that you can access an NBT Identity Badge. Please ask the appropriate NBT Manager/Research link person to sign this form and liaise with security as necessary. Please note that North Bristol NHS Trust accepts no responsibility for damage to or loss of personal property.

We may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence. Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

North Bristol NHS Trust will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport/External Researcher Information Form (ERIF) changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in North Bristol NHS Trust.

If you have any queries about the arrangements for research please contact Angelo Micciche, Research Infrastructure Manager (0117 3238601) in the first instance.

Yours sincerely

[redacted]

Adam Smardon
Senior HR Administrator

Copy: [redacted]

Enc

APPENDIX D: Reply Slip, Study 2

"Understanding the Psychological Impact of Joint Hypermobility Syndrome"

Telephone Interview Reply Slip

Please complete this reply form and return it to us in the pre-paid envelope provided. The researcher will be in touch with you shortly to discuss the study with you.

Please complete your details below:

Name: _____

Telephone Number: _____

Email address: _____

If you require any further information, please contact Sarah Bennett at [redacted]

Please return this reply slip in the enclosed pre-paid envelope.
Thank you for your interest in this research project.

APPENDIX E: Study 2: Participant Information Sheet, Study 2

"Understanding the Psychological Impact of Joint Hypermobility Syndrome"

Invitation Letter

Dear Sir or Madam,

I enclose some information about a research project we are currently conducting. You have received this information because you are a member of the Hypermobility Syndromes Association (HMSA)/ Ehlers-Danlos Support UK (EDS-UK), OR have received physiotherapy for joint hypermobility at North Bristol NHS Trust or the Royal National Hospital for Rheumatic Diseases.

I would be very grateful if you could read the enclosed information carefully before deciding whether or not to take part.

If you are interested, please could you either:

A: Complete paper copies of the participant response pack and the reply slip and **return them in the prepaid envelope provided**.

Alternatively, if you have access to the internet-

B: If you have access to the **internet**, follow this **secure password-protected link** to complete the participant response pack and reply slip online. Copy this carefully, it is **case-sensitive**: [redacted]
Your password is: zebra101

Please contact the lead researcher Miss Sarah Bennett via email (detailed below) if you have any questions about the study. If you do not wish to take part, then simply ignore this letter. Your healthcare and membership will not be affected. Thank you for your consideration.

Yours sincerely,

[redacted]

Miss Sarah Bennett

[redacted]

University of the West of England BRISTOL

Royal United Hospitals Bath NHS Foundation Trust

North Bristol NHS Trust

HMSA Hypermobility Syndromes Association

Ehlers-Danlos Support UK MAKING OUR INVISIBLE VISIBLE

"Understanding the Psychological Impact of Joint Hypermobility Syndrome"

Participant Information Sheet: Telephone Interview Phase

We are inviting you to take part in a research study. Before you decide whether or not to take part, it is important to understand what the research will involve, and why it is being conducted. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Please ask if there is anything that is not clear, or if you would like more information.

What is the purpose of the study?

- Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome Hypermobility type (EDS-HT) are conditions where some or all of the joints within your body move beyond a typical range of movement. This hypermobility is sometimes referred to as being 'double-jointed'. Hypermobility can cause joint instability and chronic pain.
- We know that physical things such as long-term chronic pain can have an impact on how you feel. The purpose of this study is to explore people's experiences of living with JHS/EDS-HT and how they cope with their condition using telephone interviews. These interviews will be **recorded**.
- The purpose of the telephone interview is to gather data. In a later phase of the study, we will use this data to choose questionnaires.
- At the end of the study we will have a greater insight into how JHS/EDS-HT makes people think and feel.
- This study is part of a PhD qualification at the University of the West of England.

Why have I been invited to participate?

- This study involves people with and without joint hypermobility in order to compare results. You will have been invited to participate either because:
  1. You have been diagnosed with Joint Hypermobility Syndrome (JHS), and/or Ehlers-Danlos Syndrome Hypermobility type (EDS-HT or EDS Type 3) and are a member of the HMSA or EDS-UK, or

you have received physiotherapy for your condition at the Royal National Hospital for Rheumatic Diseases or North Bristol NHS trust.

- You are aged 18 years or above and have **not** been diagnosed with another musculoskeletal disorder such as osteoarthritis, inflammatory or autoimmune arthritis or have been diagnosed with a different type of Ehlers-Danlos Syndrome.
- If you have been diagnosed with Fibromyalgia you **can** still take part.

Do I have to take part?

This study is designed to cause minimal difficulty to you. It is up to you to decide whether or not to take part. If you do decide to participate you will be invited to sign a consent form. You are free to withdraw your consent at any time without giving a reason and your healthcare will not be affected. After analysis of the results we will retain your anonymised data for a period of 5 years.

What happens if I decide to take part?

- If you are interested in taking part in the study, please return the reply slip in the pre-paid envelope. Alternatively, please complete and return a reply slip via the online link.
- We will contact you to answer any questions you may have about the study and ask some questions to confirm your eligibility to take part.
- We will send you some questionnaires to complete:
    - Demographic questionnaires will be used to **select** participants by age, gender and ethnic origin to gain data from under-represented groups in JHS/EDS-HT research.
    - A second questionnaire will ask you about how you feel.
- The results of these questionnaires will be analysed and we will select participants on the basis of gender, age and condition severity to make sure we include as wide a range of people as possible.
- Please note that we will only select between 15-20 people for interview. So there is a chance that you may not be included in the interviews, however we will inform you about this if that is the case.
- After all checks and questionnaires have been completed, we will arrange a telephone interview at a time convenient to you. This will be **recorded** and stored securely at the University of the West of England. More information about how your data will be stored is outlined below.

What will happen if I do take part?
Telephone Interview (approximately 45-60 minutes duration)

- If you are eligible and willing to take part in the study you will be asked some questions relating to your experiences with JHS/EDS-HT in a telephone interview.

- This telephone interview will be **recorded**.
- The telephone interview will be held at a time and place convenient to you.
- We are interested in a wide range of factors identified as relevant by other people with JHS/EDS-HT, including your experience of diagnosis, treatment, your health over time and your current mood. We are particularly interested in your thoughts, feelings and helpful or unhelpful coping mechanisms.
- The principal researcher is fully trained in talking to people about such experiences in a sensitive, non-judgemental and empathetic way.

Will my taking part in the study be kept confidential?

- Yes. We will follow ethical and legal practice and your information will be handled in confidence.
- Your participation, data and any information you give during the study will be kept confidential. Audio-recorded interviews will be password-protected at file-level and stored securely on a University password-protected server that is backed up nightly. The audio recordings will be copied from the digital recorder to the server after each day of interviews.
- Hard copies of data such as completed questionnaires, interview notes and signed consent forms will be stored in a locked cabinet in the office of the principal investigator.
- Your name and personal information will be anonymised with a code prior to analysis and writing-up results. All names, places and identifying features mentioned in the interviews will also be anonymised. Nobody will be able to identify you from your responses.

What are the possible disadvantages of taking part?

- If you take part in the telephone interview, this will take up to 1 hour. You can take a break or stop completely at any time of the interview process.
- We would like to record the telephone interview, in order to analyse and compare the experiences of other people with JHS/EDS-HT.
- The discussion of some memories may cause you to feel unhappy, such as discussions of previous hospital treatment or experiences with healthcare professionals. These questions are chosen to help us better understand the lived experiences of those with JHS/EDS-HT and find ways to help. You can stop at any stage of the interview and you can refuse to answer any questions.
- Whether you decide to take part in this research or not, your healthcare will not be affected in any way.

What are the possible advantages of taking part?

Although taking part may not benefit you directly, your participation in this study will improve our understanding of how people live and cope with JHS/EDS-HT.

What will happen to the results?

The results of this study will be published in journals and presented at conferences, which will help healthcare professionals and researchers towards better management and awareness of the effects of JHS/EDS-HT. After analysis of the results we will retain your anonymised data for a period of 5 years.

Who is organising and funding this research?

The University of the West of England is supervising the quality of the research as part of a self-funded PhD qualification.

Who has reviewed this study?

The scientific quality of the research has been reviewed and approved by the University of the West of England Faculty Research Degree Committee and the West London and GTAC Research Ethics Committee. Staff at the University of the West of England will continuously monitor the study.

How do I make a complaint?

- If you have any further questions, please contact Sarah Bennett via [redacted] or Professor Shea Palmer at
- Alternatively, you can make an independent formal complaint via the NHS Complaints Procedure. Details can be found on the NHS Choices website.

Where can I find independent information about taking part in research?

- You can contact the Research and Innovation Department at North Bristol [redacted]
- Alternatively you can contact your local branch of the NHS Patient Advisory Liaison Service (PALS) on their website: www.pals.nhs.uk.

Thank you for taking the time to consider taking part in this research project. Please keep a copy of this information sheet for future reference.

Enquiries: [redacted]

Chief Investigator
Sarah Bennett, [redacted]

APPENDIX F: Informed Consent for particiation, Study 2

University of the West of England, Royal United Hospitals Bath NHS Foundation Trust, North Bristol NHS Trust, HMSA Hypermobility Syndromes Association, Ehlers-Danlos Support UK MAKING OUR INVISIBLE VISIBLE

"Understanding the Psychological Impact of Joint Hypermobility Syndrome"

Chief Investigator: Miss Sarah Bennett

Participant ID: …….. **Initials:** …… **Date of Birth:** ……..... **DD/MM/YY**

Please **add your initials** to each point.

	Your Initials
1. I confirm that I have read and understand the information sheet dated 15th April 2016 (Version 2) for the above study and have had the opportunity to ask questions.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, with no reason, without my medical care or legal rights being affected. At the point of withdrawl I can request that my interview data is destroyed. However, after analysis it will not be possible to withdraw my data.	☐
3. I am happy for my anonymised data to be used for future research purposes. I have been assured that strict confidentiality will be maintained.	☐
4. I am happy for researchers to audio-record my telephone interview for research purposes.	☐
5. I am happy for the researchers to contact me for future research into joint hypermobility and to clarify any details with me.	☐
6. I agree to participate in the above study.	☐

Name of Participant _____ Date _____ Signature _____

Enquiries:
[redacted]

Chief Investigator
Sarah Bennett,
[redacted]

APPENDIX G: Demographic questionnaires, Study 2

"Understanding the Psychological Impact of Joint Hypermobility Syndrome"

Participant Response Pack

Section A: Your Details

This section collects demographic information about you so that we can compare your results to other people with and without joint hypermobility. Please return this pack in the prepaid envelope provided.

Today's date:	D D M M 2 0 Y Y
Date of Birth:	D D M M 1 9 Y Y

Are you a member of? ✓ *Please tick*
☐ HMSA ☐ EDS-UK
Have you been treated for hypermobility at either of these NHS trusts? ✓ *Please tick*
☐ North Bristol
☐ Royal United Hospitals, Bath

Name: _____
Phone: Home _____ Mobile _____
Email: _____

A1. Do you identify as: ☐ Female ☐ Male

A2. What is your ethnic group? ✓ *Please tick*

☐ White
☐ Mixed/multiple ethnic groups, Please specify: _____
☐ Asian/Asian British
☐ Black/African/Caribbean/Black British
☐ Other ethnic group, please specify: _____

Section B: Your Hypermobility

Please **circle your response** to each of the following 5 questions:

B1. Can you now (or could you ever) place your hands flat on the floor without bending your knees?	Yes	No
B2. Can you now (or could you ever) bend your thumb to touch your	Yes	No

forearm?		
B3. As a child did you amuse your friends by contorting your body into strange shapes OR could you do the splits?	Yes	No
B4. As a child or teenager did your shoulder or kneecap dislocate on more than one occasion?	Yes	No
B5. Do you consider yourself double-jointed?	Yes	No

Have you ever received a **formal diagnosis** (from a healthcare professional) of:

B6a. Joint Hypermobility Syndrome	Yes	No
B6b. Ehlers-Danlos Syndrome Hypermobility Type (formerly EDS-III)	Yes	No
B6c. Other connective tissue disorder Please specify: _____	Yes	No

APPENDIX H: The Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith, 1983)

Section C: Your Mood

This questionnaire helps us to understand how you are feeling. Read each sentence and place a tick ☑ on the answer that best describes how you have been feeling **during the last week**. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important.

C1. I feel tense or 'wound up'

- ☐ Most of the time
- ☐ A lot of the time
- ☐ From time to time
- ☐ Not at all

C2. I still enjoy the things I used to:

- ☐ Definitely as much
- ☐ Not quite so much
- ☐ Only a little
- ☐ Hardly at all

C3. I get a sort of frightened feeling as if something awful is about to happen:

- ☐ Very definitely and quite badly
- ☐ Yes, but not too badly
- ☐ A little, but it doesn't worry me
- ☐ Not at all

C4. I can laugh and see the funny side of things:

- ☐ As much as I always could
- ☐ Not quite as much now
- ☐ Definitely not so much now
- ☐ Not at all

C5. Worrying thoughts go through my mind:

- ☐ Most of the time
- ☐ A lot of the time
- ☐ From time to time
- ☐ Only occasionally

C6. I feel cheerful:

- ☐ Most of the time
- ☐ Usually
- ☐ Not often
- ☐ Not at all

C7. I can sit at ease and feel relaxed:

- ☐ Most of the time
- ☐ Usually
- ☐ Not often
- ☐ Not at all

C8. I feel as if I am slowed down:

- ☐ Nearly all the time
- ☐ Very often
- ☐ From time to time
- ☐ Not at all

C9. I get a sort of frightened feeling like butterflies in the stomach

- ☐ From time to time
- ☐ Not at all
- ☐ Quite often
- ☐ Very often

C10. I have lost interest in my appearance:

- ☐ Definitely
- ☐ I don't take as much care as I should
- ☐ I may not take quite so much care
- ☐ I take just as much care as ever

C11. I feel restless, as if I had to be on the move

- ☐ Very much indeed
- ☐ Quite a lot
- ☐ Not very much
- ☐ Not at all

C12. I look forward with enjoyment to things:

- ☐ As much as I ever did
- ☐ A little less than I used to
- ☐ Definitely less than I used to
- ☐ Hardly at all

C13. I get a sudden feeling of panic:

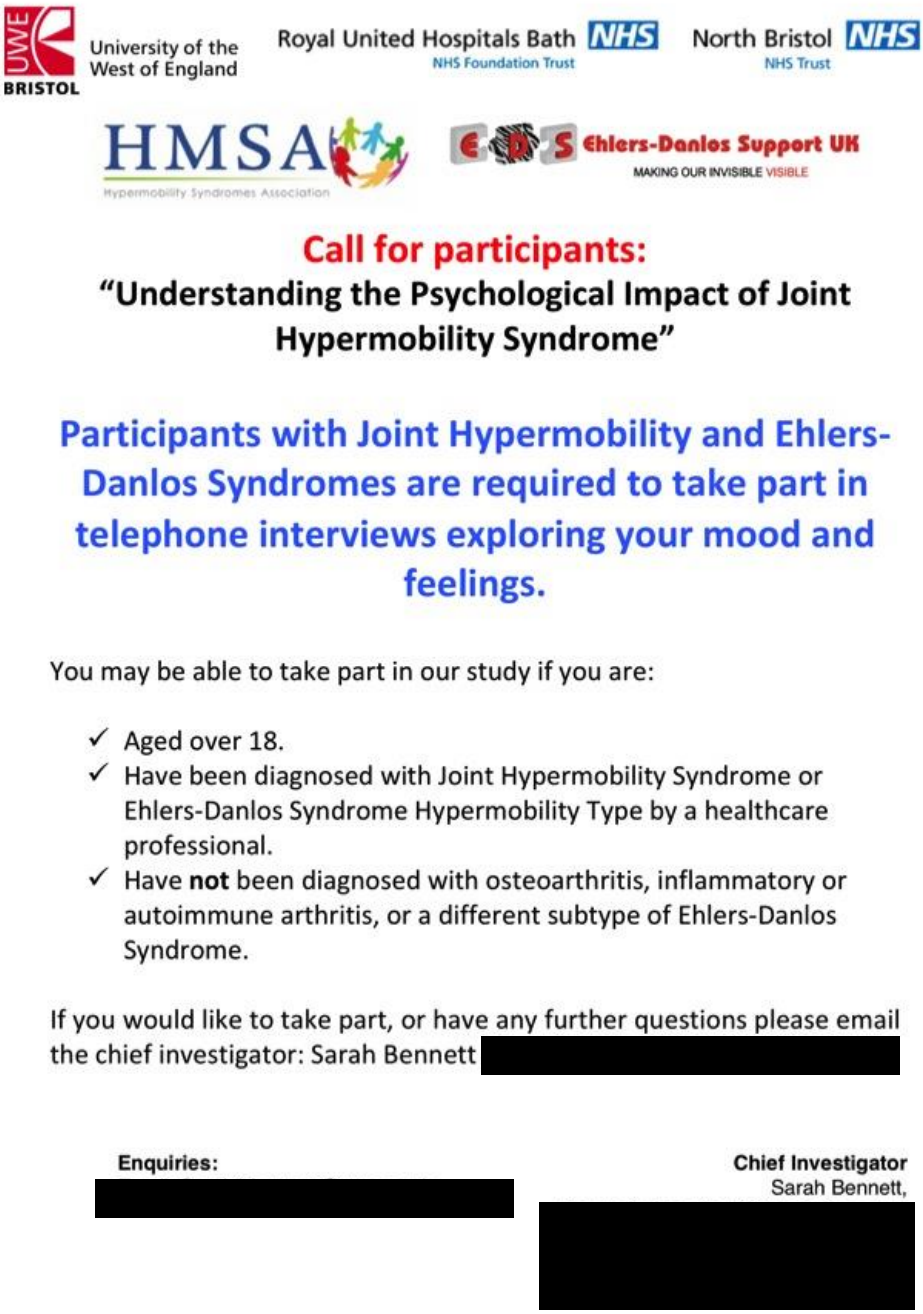
- ☐ Very often indeed
- ☐ Quite often
- ☐ From time to time
- ☐ Not at all

C14. I can enjoy a good TV or radio program or book:

- ☐ Often
- ☐ Sometimes
- ☐ Not often
- ☐ Hardly at all

THANK YOU - END OF QUESTIONS

APPENDIX I: Advertisment: Study 2



APPENDIX J: Interview protocol, Study 2

Understanding and Managing the Psychological Impact of Joint Hypermobility: Interview Topic Guide

Introduction

I would like to reiterate that everything you say in this interview will be kept confidential. Any names, places or identifying information that you give will be anonymised and nobody will be able to identify you from your answers. The questions I'm going to ask are fairly broad and wide-ranging to allow you to tell your own story. There are no right or wrong answers; I am simply interested in your experiences and your views. The first part of the interview is about your experiences of diagnosis in general. Later, I will be asking you about aspects of JHS/EDS-HT and your care. Is there anything you would like to ask me before we begin?

Journey to diagnosis

- Can you clarify for me whether your diagnosis is joint hypermobility syndrome (JHS) or Ehlers-Danlos Syndrome (EDS-HT) (or both)?
- How did you come to be diagnosed?
    - How long before you first started having symptoms and receiving your diagnosis? What age were you at diagnosis?

The impact of JHS/EDS

- What are your symptoms?
    - Physical symptoms e.g. subluxations, dislocations
    - Fatigue?
- How do you manage your day-to-day activities?
    - Do any activities that make symptoms worse? What happened?
- What impact does JHS/EDS-HT have on your education and/or work life?
- Has hypermobility had any impact on your relationships with other people, such as friends, family?
- What impact has JHS/EDS-HT had on your social and leisure activities?
- Emotional impact?

    - Anxiety? Shame Depression
- How do you feel about having EDS/JHS?
    - Has having EDS/JHS changed how you think or feel about yourself?
    - Have there been any positive impacts? (e.g. relief at diagnosis?)

Identifying coping

- Is there anything that you have tried that has had a **beneficial** impact on your condition?
    - Physical (e.g. exercises, physiotherapy, pilates, yoga etc.)
    - Emotional (e.g. relaxation, mindfulness, CBT, pain management? etc.)
- Can you say what it is about these methods has helped?
- If you had to give advice to another person about how to cope well with JHS/EDS-HT what would that be?

JHS: Poorly understood?

- Some research has suggested JHS/EDS-HT are poorly understood conditions, by healthcare professionals and others. What are your views on this?
- Have you had difficulties/benefits from the 'invisible' nature of JHS/EDS-HT?
    - With whom? (family, co-workers, doctors, strangers?)

Experiences of healthcare professionals

- What have been your experiences of healthcare professionals?
    - Doctors, physiotherapists, OT's, psychologists?
    - What kinds of treatment have you been offered?
    - Has your treatment changed following diagnosis?
- Some research suggests that healthcare professionals can struggle to know how to treat patients with JHS/EDS-HT, while others seem to be more confident. I wonder which is closer to your experience?
- Have you taken steps to educate yourself about JHS/EDS-HT and find out more about the condition? Why/Why not?

Closing –

- Is there anything else about your experiences, thoughts or feelings of living with JHS/EDS-HT that I haven't mentioned? Any questions that you thought I would ask, or wished I'd asked, but didn't?
- Thank you for taking the time to talk with me today.

APPENDIX K: Distress Protocol, Study 2

Date: _____Time: _____ Interview Number:_____ Participant Code:_____

Understanding the Psychological Impact of Joint Hypermobility Syndrome
Participant Distress Protocol

This protocol outlines the actions of the principal investigator in, during the course of the telephone interview, a participant exhibits acute distress, or the researcher is concerned that participants are finding the interview unduly stressful. All participants will be advised that they can withdraw from the study at any time without the need to provide an explanation.

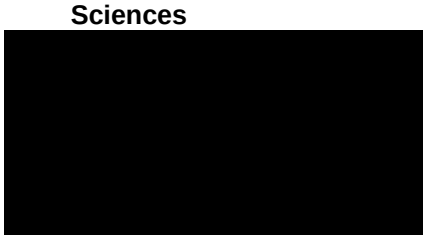
Indications of Distress During Interview	**Researcher Actions:**	**Participant Response:**	**Interview Paused or Stopped? (Y/N)**
STAGE 1 *Participant indicates that they are experiencing a high level of stress or emotional distress OR exhibit behaviours suggestive that the interview is too stressful such as:* • *Crying* • *Incoherent speech* • *Excessive nervousness*	1. Stop the interview 2. Offer support and allow the participant time for a break and to regroup. 3. Ask how the participant is feeling and whether they feel able to continue. 4. Sensitively reiterate that they can stop the interview or take a break at any time. 5. If participant feels able to continue, resume the interview. 6. If not, go to Stage 2.		
STAGE 2 *Participant feels unable to continue interview.*	1. Interview discontinued. 2. Offer, with participant consent, to follow up with either a phone call or email at a later date convenient to both parties. 3. Encourage participant to contact their GP and offer signposting to support services.	**Follow up date & time:**	
STAGE 3 *Report incident to supervisors and follow up with participant at a later date.*	4. Report incident and details to supervisors immediately. 5. Follow up with participants at the time and date agreed upon in Stage 2, by phone or by email if preferred.		

Mental Health Support Services Available:

- Improving Access to Psychological Therapies (IAPT) NHS Services for Depression and Anxiety (www.iapt.nhs.uk).
- Recommended to contact their GP and either GP-refer or self-refer to the appropriate support services.

APPENDIX L: Ethical approval of Study 3 from the UWE Faculty Research Degrees Committee (FRDC)

Faculty of Health & Applied Sciences



UWE REC REF No: HAS.18.03.128

27th April 2018

Sarah Bennett

Dear Sarah

Application title: Developing a self-management intervention to manage JHS/EDS-HT using behaviour change theory

I am writing to confirm that the Faculty Research Ethics Committee are satisfied that you have addressed all the conditions relating to our previous letter sent on 23rd April 2018 and the study has been given ethical approval to proceed.

Please note that any information sheets and consent forms should have the UWE logo. Further guidance is available on the web: https://intranet.uwe.ac.uk/tasks-guides/Guide/writing-and-creating-documents-in-the-uwe-bristol-brand

The following standard conditions also apply to all research given ethical approval by a UWE Research Ethics Committee:

You must notify the relevant UWE Research Ethics Committee in advance if you wish to make significant amendments to the original application: these include any changes to the study protocol which have an ethical dimension. Please note that any changes approved by an external research ethics committee must also be communicated to the relevant UWE committee.
http://www1.uwe.ac.uk/research/researchethics/applyingforapproval.aspx

You must notify the University Research Ethics Committee if you terminate your research before completion;

You must notify the University Research Ethics Committee if there are any serious events or developments in the research that have an ethical dimension.

Please note: The UREC is required to monitor and audit the ethical conduct of research involving human participants, data and tissue conducted by academic staff, students and researchers. Your project may be selected for audit from the research projects submitted to and approved by the UREC and its committees.

Please remember to populate the HAS Research Governance Record with your ethics outcome via the following link: https://teams.uwe.ac.uk/sites/HASgovernance.

We wish you well with your research.

Yours sincerely

[redacted]

Dr Julie Woodley

Chair

Faculty Research Ethics Committee

c.c. Shea Palmer

APPENDIX M: COM-B and TDF mapping: First results (prior to focus group discussions), Study 3.

CAPABILITY		OPPORTUNITY		MOTIVATION	
PSYCHOLOGICAL	**PHYSICAL**	**SOCIAL**	**PHYSICAL**	**AUTOMATIC**	**REFLECTIVE**
Informative JHS/EDS-HT leaflets and guidance to increase HCP knowledge and understanding. Establish and disseminate clear guidance for treating JHS/EDS-HT, including assessment, referral, & complications e.g. local anaesthetics. Training for HCP's to improve interpersonal skills. Training for patients focusing on advocacy, assertiveness and communication skills, to	Training for regarding physiotherapy techniques that recognise and accommodate poor proprioception. E.g. exercises using a mirror for reference. Training for HCP's- encouraging patients with JHS/EDS-HT to use a mirror when completing exercises. Training in pacing skills to improve boom/bust cycle of activity and reduce flare-ups in symptoms and need for excessive rest time.	Enablement: Pacing activities to reduce limits to social activity caused by symptoms. Restructure physical environment and made modifications to reduce mobility difficulties. Using behavioural modeling examples to show patients with JHS/EDS-HT how to communicate their needs to others in social situations.	Training in pacing skills to improve boom/bust cycle of activity and reduce flare-ups in symptoms and need for excessive rest time. Restrict tiring, stressful or activities with a high risk of accidental injury. Environmental restructuring- advice from a workplace occupational therapist regarding how to restructure the environment to best meet patients needs, and enable them to achieve	Educational examples of modelled behaviours (self help strategies for coping with injury and pain). Environmental restructuring and enablement: altering the physical environment, with occupational therapy input, in order to achieve tasks independently. Use of positive first-person modelling narratives that	Educational programmes for patients with JHS/EDS-HT, with a focus on self-help and coping strategies for injury or pain. Education regarding positive body image. First person modelling narratives regarding body changes with EDS. Persuasion- emphasise participant capability in social situations to

1) reduce anxiety and 2) improve interpersonal communication of their needs to HCP's and in hospital settings. Communication training for participants to 1) improve acceptance of condition and self-confidence in order to 2) explain and improve disease knowledge in others, Education for patients addressing knowledge and management of JHS/EDS-HT, pain control and self-help measures, fears about decline. Pregnancy with JHS/EDS-HT - Improved education, training and information for participants with JHS/EDS-HT regarding what to expect.	Restrict tiring, stressful or activities with a high risk of accidental injury. Model pacing behaviours. Training in Occupational Therapy methods to improve physical capability with everyday tasks- Establish feedback regarding trusted, accurate sources of information for JHS/EDS-HT.	Modeling narratives that emphasise independence from family members. Enablement of those needing accessible seating or parking - TFL Blue Badge scheme, council blue badge scheme. Restrict opportunities to compare self to others with JHS/EDS-HT on the internet by promoting reliable sources of information about JHS/EDS-HT.	their goals effectively. Identify and restrict access to unreliable information sources. Enable ease of access by providing JHS/EDS-HT information resources within an easily-located webpage or source.	address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped. Modeling of coping strategies from mothers with JHS/EDS-HT who have had children. Develop guidance templates outlining examples of increased JHS/EDS-HT symptoms and what to do, to act as a support tool.	reduce fear. Persuasion of capability regarding physical ability, to reduce fear of injury. Modeling of potential social interactions and situations, to improve confidence and reduce fear of social situations. Enablement- joint protection strategies/information for when out of the house or modeling advice for social situations. Education regarding consequences of overexertion and exacerbations of pain/fatigue.

Aims of the session 10/12/18:

A 1-1.5 hour meeting and discussion exercise to **examine** and **discuss** the compiled results of the COM-B and TDF mapping and associated modifiable behaviours.

Decisions will be made regarding which behaviours identified by the mapping process could be **modifiable** and how best to modify them.

Consideration to ensure materials are **clear**, **comprehensive** and **relevant** to the target population.

Any disagreements or factors that could apply to more than one category will be discussed as a team to reach consensus.

References:

Michie, S., van Stralen, M.M. & West, R. (2011). The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Science,* 6:42.

Key terms:

HCP: Healthcare professional

JHS: Joint Hypermobility Syndrome

EDS-HT: Ehlers-Danlos Syndrome (Hypermobility type)

TDF: Theoretical Domains Framework: Developed by experts in behaviour change, the framework was developed from a number of psychological theories to help choose of theories most relevant to behaviour change interventions. These domains can be mapped onto the Behaviour Change Wheel (BCW).

COM-B: Part of the **Behaviour Change Wheel (BCW; Michie, van Stralen and West, 2011),** a model based on the concept that **c**apability, **o**pportunity, and **m**otivation interact to generate **b**ehaviour. Surrounding this central hub is a ring of nine intervention functions to choose from. The COM-B model is made up of 6 components:

Physical capability: Physical skill (e.g. the skill to complete physiotherapy exercises)
Psychological capability: The capacity to engage in the necessary thought processes (e.g. awareness of JHS/EDS-HT symptoms.)
Physical opportunity: Opportunity afforded by the environment (e.g. being able to go running because you own trainers).
Social opportunity: Social environment that enables the behaviour (e.g. cues that prompt people to eat or be physically active)

Reflective motivation: Reflective processes involving evaluations and beliefs about capabilities or consequences (e.g. beliefs about ability to exercise with JHS/EDS-HT)
Automatic motivation: Automatic processes involving emotions and impulses that arise from conditioned behaviour (e.g. reward or reinforcement) or innate character traits.

Intervention functions of the COM-B Behaviour Change Wheel (or, what the intervention will do)

Education: Increasing knowledge or understanding.
Environmental restructuring: Changing the physical or social context.
Enablement: Increasing resources/reducing barriers to increase a persons skill/capability.
Incentivisation: Creating an expectation of reward.
Coercion: Creating an expectation of financial cost or punishment.
Modeling: Providing an example for people to aspire to or imitate.
Persuasion: Using communication to induce positive or negative feelings or stimulate action.
Training: Providing skills.

APPENDIX N: COM-B and TDF mapping: Results after research group discussion of priorities, Study 3. Amendments are in red font.

CAPABILITY	OPPORTUNITY		MOTIVATION	
PSYCHOLOGICAL	**SOCIAL**	**PHYSICAL**	**AUTOMATIC**	**REFLECTIVE**
Skills development training for patients focusing on advocacy, assertiveness and communication, to improve interpersonal communication of their needs. **Education for patients** addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures, fears about decline. **Pregnancy with JHS/EDS-HT** - Improved education, training and information for participants regarding what to expect. Establish guidance regarding trusted, accurate sources of information for JHS/EDS-HT. Training in **pacing skills** where individuals can learn to actively manage cycles of activity and rest to achieve increased participation in daily activities.	**Behavioural modeling examples** to show how to communicate your needs to others in social situations. **Modeling narratives** that emphasise independence from family members in completing daily tasks. **Environmental restructuring and enablement**: altering the physical environment, with occupational therapy input, in order to achieve tasks independently. (moved from automatic motivation)	**To safeguard from negative or unreliable information:** Identify and restrict access to unreliable information sources. Enable ease of access to reliable information within an easily-located webpage or source.	**Educational examples of behaviours**, including self help strategies for coping with injury and pain. **Positive first-person modeling narratives** that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped. Modeling of **coping strategies** from mothers with JHS/EDS-HT who have had children. Education regarding the	**Educational programmes** with a focus on self-help and coping strategies for injury or pain. **Education** to manage beliefs and perceptions about body image. **Persuasion**- Emphasising patient's **capability** in social situations to reduce fear. **Persuasion** of **capability** regarding physical ability, to reduce fear of injury. **Education** regarding consequences of

Promote information to improve **knowledge** of accessible seating or parking - TFL Blue Badge scheme, local council blue badge scheme. (moved from Social Opportunity to Psych Capability)			likelihood that their **child** will inherit JHS/EDS-HT and signposting for support. **Develop templates** outlining examples of increased JHS/EDS-HT symptoms during **pregnancy** and what to do, to act as a support tool.	overexertion and exacerbations of pain/fatigue.

APPENDIX O: Study 3: Participant Information Sheet

"Developing a self-management intervention to manage JHS/EDS-HT using behaviour change theory"

Participant Information Sheet: Nominal Group Technique Focus Group Phase

We are inviting you to take part in a research study. Before you decide whether or not to take part, it is important to understand what the research will involve, and why it is being conducted. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Please ask if there is anything that is not clear, or if you would like further information.

What is the purpose of the study?

Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome Hypermobility type (EDS-HT) are conditions where some or all of the joints within your body move beyond a typical range of movement. This hypermobility is sometimes referred to as being 'double-jointed'. Hypermobility can cause joint instability and chronic pain.

We know that physical things such as long-term chronic pain can have an impact on your feelings. An earlier part of this study explored people's experiences of living with JHS/EDS-HT, how they cope with their condition and how it made them feel.

The purpose of these focus groups is to examine and discuss behaviours that other people with JHS/EDS-HT have identified as important when managing

their condition. This will be achieved using a method called Nominal Group Technique (NGT) where you will be given options for treatment and asked to place them in order of how important they are to you. The NGT focus group will be **recorded**.

We are conducting 2 NGT focus groups with participants who have JHS/EDS-HT, and one with healthcare professionals with an interest in JHS/EDS-HT management. This data will be used in future research to develop more relevant treatments for patients with JHS/EDS-HT.
At the end of the study we will have a greater insight into which behaviour change interventions would best help others with JHS/EDS-HT, with input from participants who have the same condition.
This study is part of a PhD qualification at the University of the West of England.

Why have I been invited to participate?

This study involves both people with joint hypermobility and healthcare professionals in order to gain useful and results relevant to other people with JHS/EDS-HT. You will have been invited to participate because you have been diagnosed with Joint Hypermobility Syndrome (JHS), and/or Ehlers-Danlos Syndrome Hypermobility type (hEDS. EDS-HT or EDS Type 3), or a Hypermobility Spectrum Disorder (HSD), and are a member of the Hypermobility Syndromes Association (HMSA) or Ehlers-Danlos Support UK (EDS-UK).

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to participate you will be invited to electronically sign a consent form using your initials. You are free to withdraw your consent at any time without giving a reason and your healthcare will not be affected. After analysis of the results we will retain your anonymised data for a period of 5 years.

What happens if I decide to take part?

If you are interested in taking part in the study, please click ‘Next’ to complete the online informed consent form after this information sheet.

After completing the consent form, there are some online questions to complete to confirm your eligibility to take part:

> A demographic questionnaire will be used to **select** participants by age, gender and ethnic origin to gain data from under-represented groups in JHS/EDS-HT research.
>
> A series of 5 questions will ask you about your joint hypermobility.

The results of these questionnaires will be analysed and we will select participants on the basis of gender, age and condition severity to make sure we include as wide a range of people as possible.

Please note that we will only select between 10-15 people for the NGT focus groups. So there is a chance that you may not be included in the interviews, however we will inform you about this if that is the case.

After all checks and questionnaires have been completed, we will arrange a focus group at a time convenient to you. This will be **recorded** and stored securely at the University of the West of England. More information about how your data will be stored is outlined below.

What will happen if I do take part?

Nominal Group Technique (NGT) focus group (approximately 60-90 minutes duration)

If you are eligible and willing to take part in the study you will be invited to take part in an NGT focus group on a pre-determined date.

Travel expenses of up to £20 per person can be claimed, on submission of receipts.

The NGT focus group will be **recorded**.

You will be presented with a range of factors identified as relevant by other people with JHS/EDS-HT, including different types of treatment, their thoughts, feelings and helpful or unhelpful coping mechanisms.

We will send you this information in advance via email for you to read through and ask any questions about. On the day of the focus group, each factor will be on a laminated card.

We are interested in how changes in these factors might help people manage JHS/EDS-HT.

Your task will be to put these items in the order that you feel is most important. Later, the whole group will discuss and vote for which items they feel are most important. Everyone will have a chance to contribute equally, and further detail about the process will be provided on the day.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and your information will be handled in confidence.

Your participation, data and any information you give during the study will be kept confidential. Audio-recorded data will be password-protected at file-level and stored securely on a University password-protected server that is backed

up nightly. The audio recordings will be copied from the digital recorder to the server after each NGT focus group.

Hard copies of data such as completed questionnaires, NGT notes and signed consent forms will be stored in a locked cabinet in the office of the principal investigator.

Your name and personal information will be anonymised with a code prior to analysis and writing-up results. All names, places and identifying features mentioned in the NGT focus groups will also be anonymised. Nobody will be able to identify you from your responses.

What are the possible disadvantages of taking part?

If you take part in the focus group, this will take between 3 and 4 hours. There will be scheduled breaks and you can take a break, stretch, move around or stop completely at any time of the focus group process.

We will **record** the focus group, in order to analyse and compare the input from other people with JHS/EDS-HT, and from healthcare professionals.

Talking about some of the items may cause you to feel unhappy, such as discussions of previous hospital treatment or experiences with healthcare professionals. These topics have been chosen to help us better understand the lived experiences of those with JHS/EDS-HT and find ways to help. You can stop at any stage of the focus group and you can refuse to answer any questions.

Whether you decide to take part in this research or not, your healthcare will not be affected in any way.

What are the possible advantages of taking part?

Although taking part may not benefit you directly, your participation in this study will improve our understanding of how people live and cope with JHS/EDS-HT.

What will happen to the results?

The results of this study will be published in journals and presented at conferences, which will help healthcare professionals and researchers towards better management and awareness of the effects of JHS/EDS-HT. After analysis of the results we will retain your anonymised data for a period of 5 years.

Who is organising and funding this research?

The University of the West of England is supervising the quality of the research as part of a self-funded PhD qualification.

Who has reviewed this study?

The scientific quality of the research has been reviewed and approved by the University of the West of England Faculty Research Degree Committee. Academic staff at the University of the West of England will continuously monitor the study.

How do I make a complaint?

If you have any further questions, please contact Sarah Bennett via [redacted] or Professor Shea Palmer at [redacted]

Alternatively, you can make an independent formal complaint via the UWE Complaints Procedure, which is publicly available on the UWE website.

Where can I find independent information about taking part in research?

You can contact the Research and Innovation Department [redacted] or email [redacted]

Alternatively you can contact your local branch of the NHS Patient Advisory Liaison Service (PALS) on their website: www.pals.nhs.uk.

Thank you for taking the time to consider taking part in this research project. Please keep a copy of this information sheet for future reference.

If you require any further information, please contact the lead researcher Sarah Bennett at [redacted]

APPENDIX P: Study 3: Participant informed consent

"Developing a self-management intervention to manage JHS/EDS-HT using behaviour change theory"

Online informed consent for participation in Nominal Group Technique focus groups:

Your initials:

I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, with no reason, without my medical care or legal rights being affected. At the point of withdrawal I can request that my questionnaire data is destroyed. However, after the NGT focus group has taken place it will not be possible to withdraw my data. ☐

I agree that researchers can audio-record the focus group for research purposes. ☐

I consent to the use of my data for reporting and dissemination. Data will be psuedonymized, with personally identifiable data substituted with a value. Data will be securely stored under General Data Protection Legislation (GDPR) regulations. ☐

I agree to participate in the above study. ☐

Optional:

	Yes:	No:
I agree that the researchers can contact me for future research into joint hypermobility and to clarify any details with me.	☐	☐
I agree that my anonymised data can be used for future research purposes. I have been assured that strict confidentiality will be maintained.	☐	☐

If you require any further information, please contact the lead researcher Sarah Bennett at [redacted]

Please click "Next" to save your answers.

Thank you for your interest in this research project.

APPENDIX Q: Study 3: Participant COM-B defintions and topic guide

CAPABILITY	OPPORTUNITY		MOTIVATION	
PSYCHOLOGICAL	**SOCIAL**	**PHYSICAL**	**AUTOMATIC**	**REFLECTIVE**
Skills development training for patients focusing on advocacy, assertiveness and communication, to improve interpersonal communication of their needs. **Education for patients** addressing knowledge and management of JHS/EDS-HT, pain control, self-help measures, fears about decline. **Pregnancy with JHS/EDS-HT** - Improved education, training and information for participants regarding what to expect. Establish guidance regarding trusted, accurate sources of information for JHS/EDS-HT. Training in **pacing skills** where individuals can learn to actively manage cycles of activity and rest to achieve increased participation in daily	**Behavioural modeling examples** to show how to communicate your needs to others in social situations. **Modeling narratives** that emphasise independence from family members in completing daily tasks. **Environmental restructuring and enablement**: altering the physical environment, with occupational therapy input, in order to achieve tasks independently. (moved from automatic	**To safeguard from negative or unreliable information:** Identify and restrict access to unreliable information sources. Enable ease of access to reliable information within an easily-located webpage or source.	**Educational examples of behaviours**, including self help strategies for coping with injury and pain. **Positive first-person modeling narratives** that address some of the negative aspects of JHS/EDS-HT (depression, distress, frustration, sexual dysfunction feelings of loss) and how they coped. Modeling of **coping strategies** from mothers with JHS/EDS-HT who have had children.	**Educational programmes** with a focus on self-help and coping strategies for injury or pain. **Education** to manage beliefs and perceptions about body image. **Persuasion**- Emphasising patient's **capability** in social situations to reduce fear. **Persuasion** of **capability** regarding physical ability, to reduce fear of injury. **Education** regarding

activities. Promote information to improve **knowledge** of accessible seating or parking - TFL Blue Badge scheme, local council blue badge scheme. (moved from Social Opportunity to Psych Capability)	motivation)		Education regarding the likelihood that their **child** will inherit JHS/EDS-HT and signposting for support. **Develop templates** outlining examples of increased JHS/EDS-HT symptoms during **pregnancy** and what to do, to act as a support tool.	consequences of overexertion and exacerbations of pain/fatigue.

Key terms:

HCP: Healthcare professional

JHS: Joint Hypermobility Syndrome

EDS-HT: Ehlers-Danlos Syndrome (Hypermobility type)

TDF: Theoretical Domains Framework: Developed by experts in behaviour change, the framework was developed from a number of psychological theories to help choose of theories most relevant to behaviour change interventions. These domains can be mapped onto the Behaviour Change Wheel (BCW).

COM-B: Part of the **Behaviour Change Wheel (BCW; Michie, van Stralen and West, 2011),** a model based on the concept that **c**apability, **o**pportunity, and **m**otivation interact to generate **b**ehaviour. Surrounding this central hub is a ring of nine intervention functions to choose from. The COM-B model is made up of 6 components:

Physical capability: Physical skill (e.g. the skill to complete physiotherapy exercises)
Psychological capability: The capacity to engage in the necessary thought processes (e.g. awareness of JHS/EDS-HT symptoms.)
Physical opportunity: Opportunity afforded by the environment (e.g. being able to go running because you own trainers).
Social opportunity: Social environment that enables the behaviour (e.g. cues that prompt people to eat or be physically active)
Reflective motivation: Reflective processes involving evaluations and beliefs about capabilities or consequences (e.g. beliefs about ability to exercise with JHS/EDS-HT)
Automatic motivation: Automatic processes involving emotions and impulses that arise from conditioned behaviour (e.g. reward or reinforcement) or innate character traits.

Intervention functions of the COM-B Behaviour Change Wheel (or, what the intervention will do)

Education: Increasing knowledge or understanding.
Environmental restructuring: Changing the physical or social context.
Enablement: Increasing resources/reducing barriers to increase a persons skill/capability.
Incentivisation: Creating an expectation of reward.
Coercion: Creating an expectation of financial cost or punishment.

Modeling: Providing an example for people to aspire to or imitate.
Persuasion: Using communication to induce positive or negative feelings or stimulate action.
Training: Providing skills.

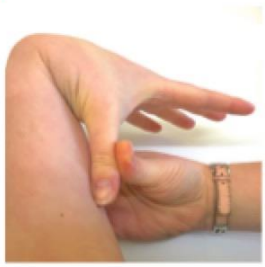
APPENDIX R: Advertisement: Study 3

HMSA Hypermobility Syndromes Association

UWE Bristol University of the West of England

EDS EHLERS-DANLOS SUPPORT UK

Are you an adult with Joint Hypermobility Syndrome (JHS) or Ehlers-Danlos Syndrome Hypermobility type (EDS-HT) OR have experience treating adult patients with JHS/EDS-HT?



We would like to invite you to take part in a research focus group. The focus group will be an opportunity to contribute to future practice for managing JHS and EDS-HT:

- The purpose of this study is to examine and discuss behaviours that other people with JHS/EDS-HT have identified as important when managing their condition.
- You will be given options for treatment and asked to vote for how important they are to you, using a wireless voting device. Later, the whole group will discuss and vote for which items they feel are most important.
- The focus group will be recorded and any responses will be anonymised.
- The focus group is expected to last for between 3-4 hours.

Event details:

[redacted]

If you are interested in finding out more, please contact the lead researcher **Sarah Bennett at**

[redacted]

APPENDIX S: Qualtrics demographic questions (Study 3)

"Understanding the Psychosocial Impact of Joint Hypermobility Syndrome"

Welcome. The following questionnaires will be used to **select** participants to take part in **focus groups**.
We will use the results to select participants on the basis of gender, age and condition severity to make sure we include as wide a range of people as possible.
The questions can be navigated using the '**Next**' and '**Back**' buttons and should take approximately **3 minutes** to complete.
Your participation, data and any information you give during the study will be kept **confidential**.

NEW PAGE

Section A: Your details

This section collects demographic information about you so that we can compare your results to other people with and without joint hypermobility.

Please complete your details below:

Your name: _____

Your date of birth: DD/MM/YY: _____

Are you a member of?

HMSA

EDS UK?

Neither

Prefer not to say

Phone number (home) _____

Phone number (mobile) _____

Email address_____

Do you identify as:

Male

Female

Other (please specify)

Prefer not to say

What is your ethnic group?

White

Asian/Asian British

Black/African/Carribean/Black British

Mixed/multiple ethnic groups (please specify) _____

Other ethnic group (please specify) _____

Prefer not to say

Section B: Your Hypermobility

Please choose your response to each of the following 5 questions:

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

2. Have you ever received a formal diagnosis (from a healthcare professional) of:

	Yes	No
Joint Hypermobility Syndrome (JHS)	O	O

Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT)	O	O
Ehlers Danlos Syndrome Type III (EDS-III)	O	O
Hypermobility Spectrum Disorder (HSD)	O	O
Hypermobility Type Ehlers-Danlos Syndrome (hEDS)	O	O

Other connective tissue disorder? (Please specify) _____

6. What year were you diagnosed (e.g. 1995)?_____

NEW PAGE

Thank you- end of questions.

If you require any further information, please contact the lead researcher Sarah Bennett at [redacted]

Please click "Next" to save your answers.

Thank you for your interest in this research project.

APPENDIX T: Amendment to Existing Research Ethics Approval, approved 11/06/19

Please complete this form if you wish to make an alteration or amendment to a study that has already been scrutinised and approved by the Faculty Research Ethics Committee and forward it electronically to the Officer of FREC

UWE research ethics reference number:	HAS.18.03.128
Title of project:	**Developing a self-management intervention to manage JHS/EDS-HT using behaviour change theory**
Date of original approval:	27th April 2018
Researcher:	*Sarah Bennett*
Supervisor (if applicable)	*Professor Shea Palmer, Professor Nicola Walsh, Dr Tim Moss.*

1. Proposed amendment: Please outline the proposed amendment to the existing approved proposal.

Proposed amendment 1: Bristol focus group participants to vote on suggested intervention items via email.

In discussion with members of the supervisory team, the decision was made to present three additional intervention options suggested by the London focus group to participants in the Bristol focus group (n=8) via email.

The London focus group voted on and ranked the ideas suggested by the Bristol group. However, as the Bristol group took place first, they have not yet had a chance to consider additional items raised by the London group. We feel that this would be much more comprehensive, by providing all

participants with the same opportunity to vote on each factor.

The additional options for intervention has been produced in a table, with the same 4 item Likert scale option as in the original focus group **[001 Voting Invitation Email V1 SB 11-06-19].**

Bristol focus group participants (n=8) will be contacted via email asking if they would like to vote on the three additional items suggested by the London group.

Each item will be explained clearly with definitions of key terms provided and participants invited to indicate their mark. If there is no response, one further email will be sent after 7 days. Thereafter, non-response will be interpreted as an unwillingness to take part and no further attempts will be made.

2. Reason for amendment. Please state the reason for the proposed amendment.

Proposed amendment 1: Bristol focus group participants to vote on suggested intervention items via email.
In discussion with members of the supervisory team, it was felt that giving the Bristol focus group participants the chance to vote on the additional interventions suggested by the London focus group would provide much more comprehensive findings.

3. Ethical issues. Please outline any ethical issues that arise from the amendment that have not already addressed in the original ethical approval. Please also state how these will be addressed.

No additional ethical issues are anticipated. As with the original application, responses will be immediately anonymised for the purposes of analysis and will not

be attributable to individual participants.

To be completed by supervisor/ Lead researcher:

Signature:	
Date:	*3/6/19*

To be completed by Research Ethics Chair:

Send out for review:	☐ *Yes* *X No*
Comments:	*These changes have a clear rationale and raise no new ethical issues so this can be approved.*
Outcome:	*X Approve* ☐ *Approve subject to conditions* ☐ *Refer to Research Ethics Committee*
Date approved:	*11th June 2019*
Signature:	*Dr Julie Woodley (via e-mail)*

Guidance on notifying UREC/FREC of an amendment.

Your study was approved based on the information provided at the time of application. If the study design changes significantly, for example a new population is to be recruited, a different method of recruitment is planned, new or different methods of data collection are planned then you need to inform the REC and explain what the ethical implications might be. Significant changes in participant information sheets, consent forms should be notified to the REC for review with an explanation of the need for changes. Any other significant changes to the protocol with ethical implications should be submitted as substantial amendments to the original application. If you are unsure about whether or not notification of an amendment is necessary please consult your departmental ethics lead or Chair of FREC.

APPENDIX U: Presentations and awards

CONFERENCE PRESENTATIONS

Palmer, S., Alexander, C., **Bennett, S.E,** Simmonds, J. (2019) "*Managing Complexity: Understanding and managing syndromic joint hypermobility in adults. The psychosocial impact of of Joint Hypermobility and Ehlers-Danlos Syndromes"* Platform presentation, Physiotherapy UK Symposium, 1st November 2019.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2019) "*Developing a self-management intervention to manage symptomatic joint hypermobility: An analysis informed by behaviour change theory."* Poster presentation, Centre for Health and Clinical Research (CHCR) Conference - **Nominated** for poster prize tour.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2019) "*Understanding the psychosocial impact of Joint Hypermobility and Ehlers-Danlos Syndrome."* Health and Applied Sciences Postgraduate Research Conference, 12th June 2019. **Awarded**: Second Best Oral Presentation Prize.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2019) "*The psychosocial impact of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome (Hypermobility Type)"* - Platform presentation, CHCR Seminar 14th February 2019.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2018) "*The psychosocial impact of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome (Hypermobility Type): A qualitative interview study."* - Poster presentation, The Ehlers-Danlos International Symposium, Ghent, Belgium, 28th September 2018.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. Bowie, R., De Grave, T., Johnson, J., Johnson, R., & Thomas, R. (2018) *"Prevalence of self-reported anxiety and depression in individuals with Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome (Hypermobility Type; EDS-HT).*" - Poster presentation, The Ehlers-Danlos International Symposium, Ghent, Belgium, 28th September 2018.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2018) "*Adult's experiences of Joint Hypermobility and Ehlers-Danlos Syndromes: A systematic review and thematic synthesis of qualitative studies."* - Poster presentation, The Ehlers-Danlos International Symposium, Ghent, Belgium, 28th September 2018.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2019) "*Understanding the psychosocial impact of Joint Hypermobility and Ehlers-Danlos Syndrome (Hypermobility Type): Findings to date and future plans."* Health and Applied Sciences Postgraduate Research Conference, 22nd June 2018. **Awarded**: Best Oral Presentation Prize.

Bennett, S.E., Walsh, N., Moss, T. and Palmer, S. (2018) "*The psychosocial impact of Joint Hypermobility Syndrome and Ehlers-Danlos Syndrome (Hypermobility Type): A qualitative interview study.*" - Poster presentation selected for the '*Winds of Change'* poster tour, European League Against Rheumatism (EULAR) annual conference, Amsterdam, Netherlands, 14th June 2018.

Bennett, S.E. (2017) "*Understanding the Impact of Joint Hypermobility"*. UWE Vitae Three Minute Thesis (3MT) National Semi-Finalist, July 2017. **Awarded**: UWE First Place Prize and UWE People's Choice Awards.

Bennett, S.E., Walsh, N., Moss, T. & Palmer, S. (2016) "*Understanding the Cognitive and Behavioural Impact of Joint Hypermobility Syndrome*" – Poster presentation, South West Doctoral Training Centre (SWDC) 'Inspiring Research' Conference, The University of Exeter, UK. 6th November 2016. **Awarded**: Second Best Poster Prize.

Bennett, S.E. (2015) *"If You're Hypermobile and You Know it, Clap Your Feet: Understanding the Psychological Impact of Joint Hypermobility"* – Platform presentation, Soapbox Science Bristol 15th July 2015.

HONOURS & AWARDS

2016 **Second Best Poster Prize**
SWDTC Inspiring Research Conference, The University of Exeter.

2017 **The People's Choice Award**
UWE Vitae Three Minute Thesis (3MT), Bristol.

2017 **First Place Prize**
UWE Vitae Three Minute Thesis (3MT), Bristol.

2018 **Best Oral Presentation**
UWE Faculty of Health and Applied Sciences (HAS) Postgraduate Research Conference, Bristol.

2019 **Second Best Oral Presentation**
UWE HAS Postgraduate Research Conference, Bristol.

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