The lived experience of Joint Hypermobility and Ehlers-Danlos Syndromes: A systematic review and thematic synthesis.

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Background: Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome (EDS) are heritable connective tissue disorders characterised by joint instability, pain, anxiety, depression and poor quality of life. However, peoples' lived experiences are not well understood.

Objective: To understand the lived experiences of people with JHS and EDS.

Methods: A systematic review was conducted using PRISMA guidelines. Critical appraisal and a thematic synthesis of participants' lived experiences was conducted. Eight online databases were searched from 1990 to February 2018: AMED, CINAHL, EMBASE, MEDLINE, PubMed, PsychINFO, SPORTDiscus and the Cochrane Library. Eligibility criteria were: 1) People with either JHS or EDS, clearly distinguished from generalised joint laxity; 2) Qualitative studies, or mixed qualitative and quantitative studies with qualitative data reported independently; and 3) Published in English.

Results: A total of nine studies were included. Five main themes were identified: 1) Lack of professional understanding; 2) Restricted life; 3) Social stigma; 4) Trying to 'keep up'; and 5) Gaining control. The implications of these results are explored.

Conclusions: Further qualitative research is required to examine the impact of JHS/EDS on a wider range of participants and in greater depth.

Keywords: Hypermobility; Ehlers-Danlos; qualitative; systematic review; thematic synthesis; lived experience.

Introduction

Joint Hypermobility Syndrome (JHS) and Ehlers-Danlos Syndrome (EDS) are heritable disorders of connective tissue [1]. Connective tissue acts like a 'glue', supporting and binding together various structures within the body. The defects in connective tissue affect the skin, blood vessels and ligaments [2, 3]. Symptoms include joint instability, increased range of movement, easy bruising and joint pain [4]. Increased incidences of fibromyalgia [5], dysautonomia [6], and urinary [7] and gastrointestinal problems [8]

have also been reported. EDS has 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 [3]. International classification for Ehlers-Danlos Syndromes has recently been revised, 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 [9]. Historical and geographical variations in diagnostic criteria and nosology for JHS and EDS can make comparing research difficult. At the time of the review the revised 2017 nosology had yet to been published. As all the studies had been conducted prior to the changes in nosology, all still used the terms JHS, EDS and EDS-HT, therefore these were the terms used throughout the review For consistency, we 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 [10]. Literature specifically relating to EDS estimates a frequency of approximately 1 in 5000 [11] but actual incidence within the population has yet to be studied [12].

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 [13, 14]. The multifactorial impact of JHS and EDS can lead to poor health-related quality of life [15], and restricted physical and psychological functioning [16]. 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 [17].

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 [18, 19, 20]. 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 [18, 19, 20]. Therefore, the purpose of this systematic review is to understand the lived experiences of people with JHS and EDS using thematic synthesis.

Materials and Methods

Information Sources

Eight online databases were searched (AMED, CINAHL, EMBASE, MEDLINE, PubMed, PsychINFO, SPORTDiscus and the Cochrane Library) from January 1990 to February 2018. The Open Grey database was also searched for unpublished literature. The search strategy is available in Appendix A. 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.

Study Selection & Data Extraction

A process described by Dundar and Fleeman [21] 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, and the reasons for exclusion are listed in Figure 1. Descriptive data regarding the sampling procedure, participants, data collection method, data analysis method, major and minor themes were extracted.

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 laxity (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 [17, 22]. Therefore the inclusion criteria were broadened to include participants of all ages with all EDS subtypes.

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 [23] (see Table 2). 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) [23]. To appraise the overall methodological quality, each study was assigned a numeric quality value based on their CASP score [24], 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. 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 [25]

Thematic Synthesis

The results sections and any additional qualitative data files [26] from each of the identified final papers were imported verbatim into NVivo 10 (QSR International, Melbourne, Australia) [27], as recommended by Thomas and Harden [20]. Where opinions of both healthcare professionals and patients had been sought [26], 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 [20]. 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.

Results

Included Papers

The screening process for the selection of suitable articles is detailed in Figure 1.

Study Characteristics

The majority of included papers had been published within the last 3 years (six of the nine, see Table 1). Papers were conducted in the United Kingdom [26, 28, 29, 30, 31], United States [17, 32], Belgium [33] and Sweden [22]. Four papers used clinically confirmed diagnosis [26, 29, 31, 33]; all others relied upon self-reported diagnosis. Four of the included papers used focus groups [26, 29, 32], three used interviews [22, 28, 33] and two used written questionnaire methods to gain feedback [17, 34].

Methodological Appraisal

The aims of the included papers were to describe peoples' experiences [17, 31], lived experiences [29] perceptions of daily life with EDS [22], lived experiences concerning diagnosis, daily life with EDS-HT and becoming a mother [33] decisions about activity [28], views of physiotherapy [26] and experiences of physiotherapy [30, 32, 34].

Three of the included papers were associated with a large randomized controlled trial (RCT) of physiotherapy for adults with JHS [31]. Two of the three RCT papers [26, 29] 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 [26] and their lived experiences of JHS [29]. 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 [32], such as the Ehlers-Danlos National Foundation (EDNF) [17], Flemish Association for Ehlers-Danlos Syndrome [33], Hypermobility Syndromes Association (HMSA) [26, 29, 34], Ehlers-Danlos Support UK (EDS-UK) [30] or from EDS conferences [22]. Other sources included a pain management clinic [28], medical genetics clinic [32] and physiotherapy services [26, 29, 31, 32].

The results and associated criteria for the CASP-based critical appraisal are summarised in Table 2. 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 [26, 29, 33, 34].

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 2). For each theme, quotations have been provided from included papers. Illustrative quotes representative of each theme are also presented in Table 3.

Lack of Professional Understanding

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*" [31], "*all in your head*" [17] or "*there must be something wrong in your mind*" [22]. Many were labelled: "*psychosomatic*" [22] "*self-inflicted Munchausen Syndrome*" [17] or "*malingerer*" [22]. Some participants did not feel believed by healthcare professionals "*it's…Psychological and you… just need to be a bit braver*" [26]. Many spoke of relief at discovering their diagnosis [31], "*that helped me hugely psychologically*" [29] 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 [33]. 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*." [32].

Negative Attitudes of Healthcare Professionals

Due to easy skin bruising, relatives were often accused of harming the patient with JHS or EDS [17, 22]. 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 [17]. Patients described physiotherapy with inexperienced practitioners as "*useless*", "*diabolical… No help whatsoever*" [34], many felt that their physiotherapists had "*given up*" [31] and reported that exercises had worsened their pain or led to further injuries [32].

Fear of treatment

Many with JHS and EDS reported a poor reaction to local anaesthetics, thought to be due to the underlying collagen defect [35]. 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*" [22]. Understandably, distressing experiences in addition to specialists who may be "*dismissive*" of patients' symptoms [32] led to great fear of healthcare professionals, treatments and hospitals. However, this could result in participants not getting the medical care they needed: "*I have stopped seeing doctors … I would rather suffer!*" [17].

Social Stigma

Negative attitudes of others

Participants were fearful of others' reactions when disclosing their JHS or EDS; only describing it vaguely [33]; "*If it gets around that I have EDS, it might mean a change in my situation at work*" [22]. 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'*" [29]. Others were reluctant to appear to be complaining all the time [33]. Participants spoke of being considered "*freaks*" [22] due to their hypermobility and stretchy skin. These

negative attitudes were thought to be due to others' lack of knowledge and understanding [33]. As children, participants were criticised by teachers for "*not performing as expected*" [22]. 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'* [29]. Some speculated whether "*it would be better to have an amputated leg, so that people could see that I'm struggling.*" [33].

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 [22]. Some feared the reactions of others [33]. This was used as a means of gaining control, avoiding being seen as "*the odd one out*" [29] 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"* [28]

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*" [29]

Negative attitudes towards self

Those who had negative experiences with healthcare professionals felt insecure [22] and "*inferior*" [17]. The differences in their physical appearance made participants feel "*embarrassed*" [22], "*ugly*" [22] and "*more ill than human*" [33]. 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 [28].

Restricted Life

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*" [28].

None had a regular structure for managing fatigue [33]. Participants' activities could be very limited on the days that they were in pain, but on better days they could "*jump over small houses*" [22]. 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*" [33]. 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.*" [28]. 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.*" [28].

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 [22]. 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 [22]. Chronic daily pain associated with EDS also limited participation in hobbies [31, 33], social activities [22, 33] and restricting what participants could choose regarding education and job

opportunities [22]. Frustratingly, some participants were required to readjust their career plans [22]. Others described retraining into different roles, making adaptations to their work, switching to part-time work, or stopping completely [28].

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*." [28]. 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."* [28].

"*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*." [28] 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"* [29]. 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!"* [22].

Trying to "Keep Up"

Depending on others

"Keeping up" with others who did not have JHS or EDS was physically and emotionally "*draining*" and "*difficult*" for participants [22]. 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 [29, 33]. Participants

had to restructure activities and depend on those around them for help to manage daily life [22, 33], 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*" [28]. Having an understanding partner and family was cited as a great source of support, helping to reduce feelings of guilt [33].

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 [36]. One woman defended her decision to never become pregnant, as she did not want to: "*walk around terrified for nine months*" [22]. 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.*" [22]. 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"* [33]. 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*" [33].

Gaining Control

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"* [26]. 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*." [26]. Participants described a cycle of decline as recommended exercises could make their pain "*feel* WORSE" [34] "*and then the treatment's over because you only get a few sessions*" [26]. In contrast, "*Hands-on*" [34] "*whole body*" [32] 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*" [29]; *"…It has made all the difference*" [34]. 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." [34].

Participants cited a holistic understanding of "*both me as a person and my physical condition*" as making the relationship between patient and physiotherapist work [34]. Recognizing 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.*'" [31].

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 [22, 33]. Parents were also conflicted in whether to protect their children from injury or encourage them to take on activities without fearing their condition [22, 33]. Mothers expressed a need to act as a positive role model for their children [31, 33]; actively engaging with their children gave participants an incentive to be active, and took their mind off their illness [33]. Being able to satisfy the needs of their family and children contributed positively to their identity as a '*good mother*' and boosted self-esteem [33].

Redefining normality

While participants accepted the lifelong nature of their condition as "*you're going to have it forever*" [26]; "*there is no cure for it*" [33], many found ways to pace their activities to "*live with pain that comes and goes*" [22]: "*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*" [29].

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*" [28], "*you're probably going to be like this always, you need to think of different ways to manage different things"* [26]. 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*" [26]. 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" [26].

Discussion

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 professional understanding and empathy from healthcare professionals involved in their care and from their friends and family, largely due to the invisible nature of the condition. Participants mentioned the need for increased awareness and coverage of JHS and EDS, and associated issues with local anaesthetics, specifically for healthcare professionals [17, 22]. Studies have indicated a lack of training in JHS/EDS for primary-care doctors and other healthcare professionals such as physiotherapists [1]. Although a recently published Royal College of General Practitioners (RCGP) EDS toolkit has made great efforts to improve awareness of JHS/EDS amongst UK GP's, [37] there is still much work to be done in this area to improve recognition of JHS and EDS.

Many hid their condition from others in order to appear 'normal', but this was exhausting physically and emotionally 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 catastrophizing attitudes to pain [38]. In order to reduce negative feelings, a common stigma management strategy involves patients disclosing their condition, with the aim to educate others and improve understanding [39, 40, 41]. Although no intervention for JHS/EDS related stigma currently exists, training in communication skills at an

individual level may have positive educational effects; improving participant'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 in others, which can increase patients own self-confidence and self-esteem [42]. Similarly, after potentially facing disbelief from healthcare professionals, the psychosocial impact of stigma within a JHS/EDS population needs to be considered by clinicians when working with this patient population.

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. While an intervention has not been developed for this population, 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 [43]. Evidence from RA literature indicates that employing coping strategies such as planning and adjusting daily activities and using assistive devices to be important strategies for adapting to pain [44]. 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 and childbearing in Hypermobile Ehlers-Danlos Syndrome have shown mixed results. While recent papers have shown comparatively positive results for women with JHS/EDS-HT with few complications associated with pregnancy [45], some studies have indicated risks such as rapid labour and delivery [46], increases in joint laxity and pain [47]. For these

reasons, personalised approaches to maternity care and planning have been recommended in order to ensure evidence-based best practice in maternity care [48]. Where participants with JHS/EDS had affected children, many acted as role models to their children, seeking to better control their child's treatments and management. For patients, discovering a pattern of heritable genetic disease in their family can create fear of the future [49]. However, awareness of potential genetic relationships can also give an individual a sense of mastery and control over their condition and its associated treatment. For those with affected family members, as in this case, individuals can appreciate that they are not alone in their experiences of the shared condition [49].

Strengths and limitations

To ensure validity of findings, a second reviewer independently reviewed two of the included papers for methodological quality. The review included EDS and JHS related qualitative research from a range of countries with participants of both genders from children to adulthood. 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 (CASP scores ≥8).

Participants average ages in included studies varied from an average of 33 years [31] to 43.5 years [17] (see Table 1). The studies reported age somewhat differently; by decades [17], In one study only the range, not the mean age was indicated [22] and in another participants ages were not disclosed [34]. Not stating participants age range, mean age or standard deviation can make it difficult to compare results between studies. In addition, as joint laxity is known to decrease with age [50, 51, 52, 53], 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 [17, 22] 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.

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 [26, 29, 31, 33] 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) [4]. 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 [4]. Despite studies suggesting that the 5PQ has been shown to have conflicting evidence in terms of reliability [54] 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.

Implications for research

The emotional and physical impact of JHS and EDS on adults and children 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. In addition, 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 [14]. 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 [26, 33, 55, 56]. In addition, 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 [10], 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.

Conclusion

The themes identified in this review provide new insight into the lived experience of adults and children with JHS and EDS. However, the results of this review may not have covered all factors relevant to the lived experience and impact on individuals. Further in-depth research is required, perhaps in the form of individual interviews with

participants who have JHS and EDS, in order to gain a more in-depth insight into their experiences of their condition.

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Declaration of interest statement

The authors have no conflict of interest.

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Appendix A

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”.

Search strategy:

("Hypermobility" OR "Joint Hypermobility" OR "Ehlers-Danlos") AND ("personal reflection" OR "lived experience" OR "qualitative" OR "focus group" OR "phenomenology" OR "personal experience" OR “interview”)

Limits: Papers published January 1990 - February 2018.

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

Appendix B: PRISMA 2009 Checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	N/A
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17-19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 For more information, visit: **www.prisma-statement.org**.Page 2 of 2

Tables

Table 1: Methodological details and themes of included papers

First author	Year	Country where research conducted	Diagnosis	Sample size (n)	Sex and Age	Sampling procedure	Data collection	Data analysis	Themes identified
Berglund [22]	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 [17]	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 [32]	2016	United States	JHS/EDS-HT	13	9 women 3 men (mean age 40.5 yrs, range 28 - 57)	Opportunity sample from an adult 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.
De Baets [33]	2017	Belgium	EDS-HT	10	10 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 behavior; 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 [26]	2016	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 [31]	2016	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.
Schmidt [28]	2015	United Kingdom	JHS	11	11 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 [34]	2017	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 [29]	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.

Table 2**:** Methodological rigour of included papers, appraised using the CASP checklist for qualitative papers.

Study first author surname	Year	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 [22]	2000	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	9 High
Berglund [17]	2010	Yes	Can't tell	Yes	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	8 High
Bovet [32]	2016	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	8 High
De Baets [33]	2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
Palmer [26]	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
Palmer [31]	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
Schmidt [28]	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
Simmonds [34]	2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 High
Terry [29]	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.

Table 3: Illustrative quotes from the five main themes 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" [22] "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" [17] I hate getting that vibe from people…I'm the last person who would want to make this up! [32] "My experience is that the PTs [Physical Therapists] just don't know about [EDS]." [32] "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." [31]	[17, 22, 28, 29, 31, 32, 34]
Long journey to diagnosis:	"It takes so many years to get diagnosed" [26] "I just needed to see somebody who knew what we were dealing with. I didn't want to be the educator." [32] "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." [17] "It was not until some years later that we met a doctor who knew that it was EDS and explained it to us." [22] "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 [33]	[17, 22, 26, 32, 33]
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." [22] "To get stitches is horrible when they do not know how to take care of me." [22] "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." [17]	[17, 22, 32]
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.'" [28]	[22, 28, 29, 33]
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." [22]	[22, 28, 29, 33]

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." [28] "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." [29]	[22, 26, 28, 33]

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] "It's on your mind the whole time because I'm constantly thinking about where my hands and feet are" [29] "I just avoided, avoided exercise I suppose, and avoided, sort of, exacerbating it" [31]	[22, 28, 29, 31]
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." [22] "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" [31]	[22, 28, 29, 31, 33]
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" [22] "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." [22] "One day you can be very indisposed and the next day you can jump over small houses" [22] "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." [33] "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" [31]	[22, 26, 28, 29, 31, 33]

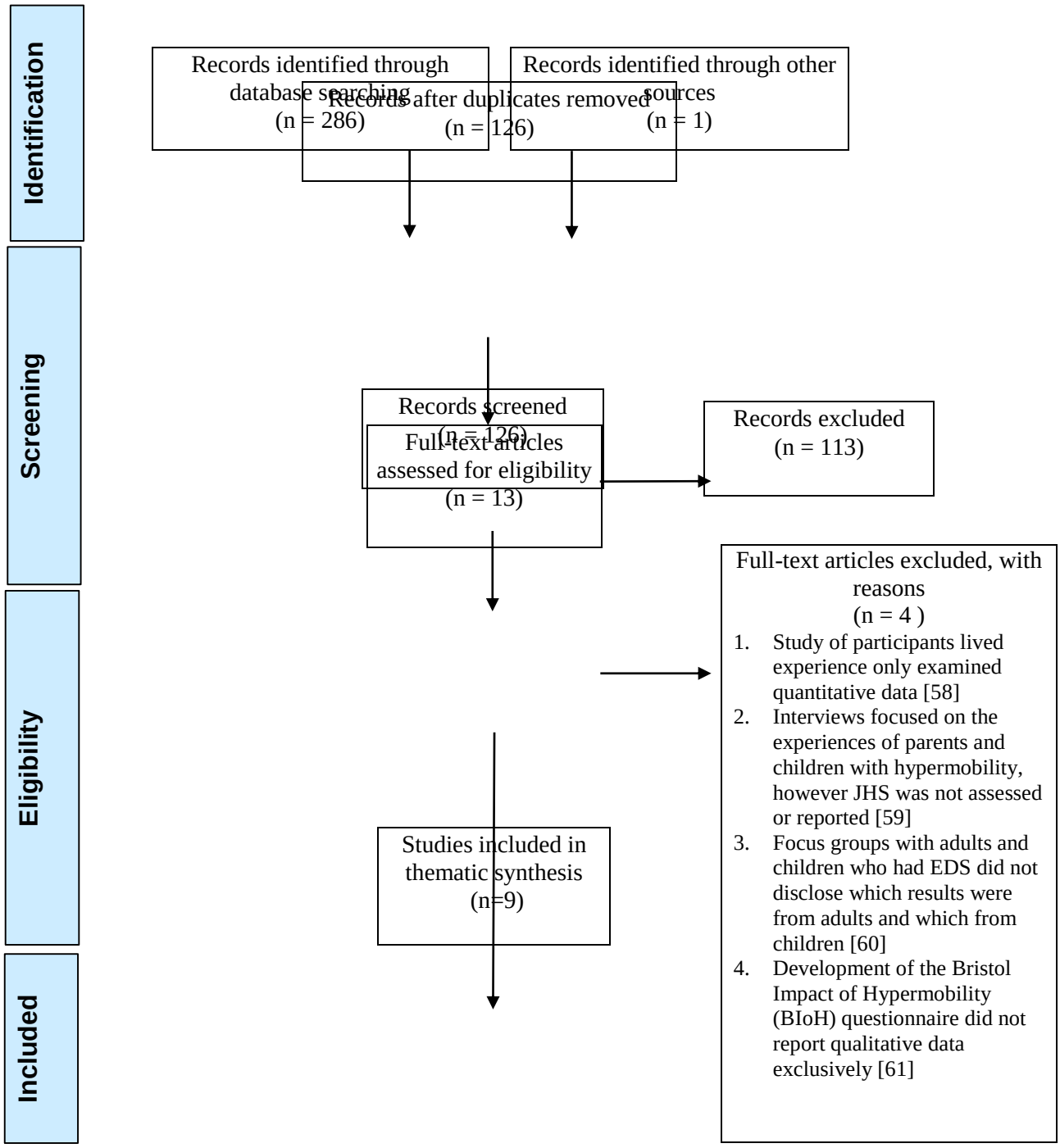
Theme and subthemes	Illustrative Quotes	References containing relevant data
Trying to "keep up"		
Depending on others:	"Something that is potentially high risk of dislocation then it's just not worth doing it, because then you got to take someone's time getting you to the hospital, so they've got to stop doing what they want to be doing, you got to waste someone's time the next day looking after me and the baby. It's just not worth it, so you just don't do it." [28] "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" [22]	[22, 26, 28, 29, 33]
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." [33]	[22, 33]

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." [32]	[26, 29, 31, 32, 33, 34]

	"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" [26]	
	"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" [26] "So could they not do a package where you actually went back every six months to see somebody regardless of how you were feeling?" [26] "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." [34] "I'm not a normal person, I don't have the joints of a normal person, so that isn't actually relevant to me" [31]	
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" [22] "You know what kind of pain your children will suffer, and you know they can't escape it" [33] "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" [33] "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" [31]	[22, 31, 33]
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." [26]	[22, 26, 28, 29, 33]
	"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." [26] "You won't be fine, not completely." [26] "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." [29]	

Figures

Figure 1: Flow diagram of study selection, following PRISMA guidelines [57]



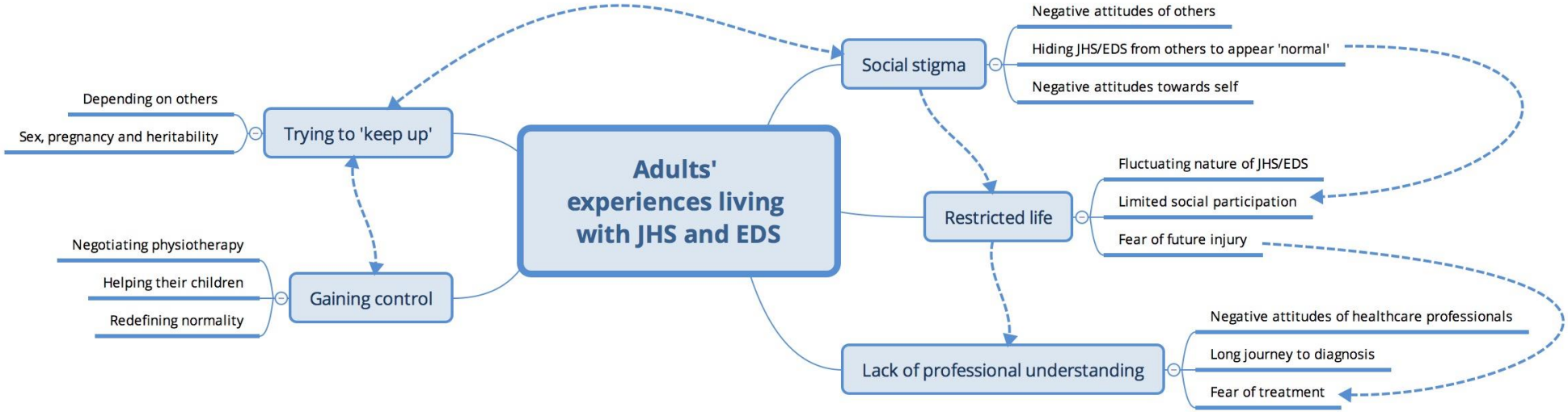


Figure 2: Thematic schema illustrating the five main themes and fourteen subthemes. Arrows represent links between themes and subthemes. Abbreviations: EDS = Ehlers-Danlos Syndrome, JHS=Joint Hypermobility Syndrome

Figure Captions

Figure 1: Flow diagram of study selection, following PRISMA guidelines [57]

Figure 2: 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