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Balancing Risk and Benefit: Is Physical Activity Protective or Harmful in Hypermobile Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorders?

Zofia Golińska, ORCID https://orcid.org/0009-0009-0598-5463

E-mail zofiagollinska@gmail.com

Ludwik Rydygier Specialist Hospital in Kraków, Kraków, Poland

Maciej Tomasz Zając, ORCID https://orcid.org/0009-0008-6851-7512

E-mail maciej.t.zajac@gmail.com

Independent Public Health Care Center in Myślenice, Myślenice, Poland

Julia Rurkowska, ORCID https://orcid.org/0009-0009-9103-3740

E-mail j.e.rurkowska@gmail.com

Independent Public Health Care Center in Myślenice, Myślenice, Poland

Krzysztof Drelich, ORCID https://orcid.org/0009-0007-3710-8380

E-mail krzy.drelich@gmail.com

The University Hospital in Krakow, Kraków, Poland

Jakub Polczyk, ORCID https://orcid.org/0009-0000-9767-9352
E-mail jakub.polczyk@protonmail.com
Independent Public Health Care Center in Myślenice, Myślenice, Poland

Filip Maciej Ogorzałek, ORCID https://orcid.org/0009-0003-2537-7971
E-mail filipogorzalek@outlook.com
Independent Public Health Care Center in Myślenice, Myślenice, Poland

Przemyslaw Rajzer MBChB, ORCID https://orcid.org/0009-0008-6925-8727
E-mail prajzer@gmail.com
Provincial Specialist Hospital in Wroclaw, Poland

Wojciech Deptuch, ORCID https://orcid.org/0009-0003-9151-4583
E-mail w.deptuch@interia.pl
Stefan Żeromski Specialist Hospital Independent Public Health Care Centre in Krakow, Kraków, Poland

Wiktor Szczuciński, ORCID https://orcid.org/0009-0003-9566-0959
E-mail wiktor.szczucinski1@gmail.com
University Hospital in Krakow, Kraków, Poland

Paweł Krzysztof Moćko, ORCID https://orcid.org/0009-0003-4984-9013
E-mail mockopawe@gmail.com
Independent Public Health Care Institution of the Ministry of the Interior and Administration in Krakow, Kraków, Poland: Krakow, Lesser Poland, PL

Corresponding Author
Zofia Golińska, E-mail zofiagollinska@gmail.com

ABSTRACT

Background. Hypermobile Ehlers–Danlos syndrome (hEDS) and hypermobility spectrum disorders (HSD) are heritable connective tissue disorders characterized by generalized joint hypermobility, joint instability, chronic musculoskeletal pain, and variable systemic involvement. hEDS is the most common EDS subtype, while HSD includes individuals with symptomatic hypermobility who do not meet hEDS criteria. Both conditions share overlapping clinical features and are diagnosed clinically. Patients often experience pain, fatigue, functional limitations, autonomic symptoms, and substantial psychological burden.

Aim. This narrative review evaluates current evidence on physical activity in hEDS/HSD, focusing on the balance between potential benefits and risks.

Material and methods. A literature search was conducted in PubMed and Google Scholar using the keywords "Ehlers-Danlos syndrome" and "physical activity." English-language studies published from 2015 onwards were included, with additional reference screening.

Results. Physical activity in hEDS/HSD is shaped by interacting physiological, psychological, and biomechanical factors. Chronic pain, fatigue, autonomic dysfunction, impaired proprioception, and reduced muscle strength limit exercise tolerance and promote inactivity. Psychological distress and fear of symptom exacerbation further reduce participation. However, tailored exercise and multidisciplinary rehabilitation are associated with improvements in pain, joint stability, physical function, and quality of life. Evidence regarding injury risk is inconsistent, suggesting outcomes depend on exercise type, intensity, and individual characteristics.

Conclusion. The impact of physical activity in hEDS/HSD is variable. Individualized, supervised, multidisciplinary rehabilitation may improve pain, stability, and quality of life despite underlying vulnerabilities. Current evidence remains limited and heterogeneous, highlighting the need for further high-quality research.

Keywords: Ehlers-Danlos syndrome, hypermobility spectrum disorders, joint hypermobility, physical activity, exercise

1. Introduction

Ehlers–Danlos Syndrome (EDS) is a heterogeneous group of inherited connective tissue disorders characterized by joint hypermobility, skin hyperextensibility, and variable systemic involvement. The 2017 International Classification of the EDS revised previous nomenclature and diagnostic frameworks, defining 13 distinct subtypes and introducing clearer criteria to improve diagnostic precision and clinical consistency [1]. Within this framework, hypermobile EDS (hEDS) was retained as a clinically defined subtype without an identified monogenic cause, while hypermobility spectrum disorders (HSD) were introduced to describe individuals with symptomatic joint hypermobility who do not fulfil all hEDS criteria [2].

hEDS is the most common subtype of EDS and is characterised by generalized joint hypermobility, joint instability, musculoskeletal pain, and soft tissue manifestations, often accompanied by multi-system symptoms including fatigue and autonomic dysfunction. It typically follows a chronic and variable course, with symptoms that may evolve over time and contribute to progressive functional impairment [3]. Despite being classified as a rare disorder in some healthcare settings, hEDS is increasingly recognised as relatively prevalent among symptomatic hypermobility conditions, though its true frequency remains uncertain.

The 2017 criteria were developed to improve diagnostic specificity and reduce heterogeneity in research cohorts; however, they also highlighted a clinical spectrum in which hEDS and HSD share overlapping features and symptom burden [1,2]. Importantly, both conditions are diagnosed clinically, as no validated molecular biomarker currently exists, complicating clear separation between pathological and benign joint hypermobility states [2].

Within this context, physical activity presents a clinical dilemma. While exercise is generally considered beneficial for musculoskeletal health, in individuals with hEDS/HSD it may potentially exacerbate joint instability and pain due to underlying connective tissue fragility. Conversely, appropriately prescribed exercise may improve proprioception, muscle strength, and joint stability, potentially reducing injury risk and symptom severity.

Therefore, understanding whether physical activity acts as a protective or harmful factor in hEDS and HSD is essential for developing evidence-based rehabilitation and management strategies in this growing patient population.

The aim of this narrative review is to critically evaluate the current evidence on the role of physical activity in individuals with Ehlers-Danlos syndrome and hypermobility spectrum disorders, with particular emphasis on balancing potential benefits and risks.

2. Research materials and methods

A comprehensive literature search was performed using the PubMed and Google Scholar databases, employing combinations of the keywords “Ehlers-Danlos syndrome” and “physical activity.” Studies published in English including meta-analyses, systematic reviews, scoping reviews, clinical trials, original research articles, case reports and case series were considered, with inclusion limited to papers published from 2015 onwards. Additionally, the reference lists of the selected articles were manually screened to identify further relevant studies.

3. Research results

3.1. Pathophysiological barriers to physical activity

Patients with hypermobile Ehlers-Danlos syndrome (hEDS) and hypermobility spectrum disorders (HSD) experience a broad spectrum of symptoms that collectively contribute to significant functional impairment. Chronic musculoskeletal pain is one of the most prevalent features and is increasingly recognized as multifactorial, involving not only peripheral mechanisms but also altered central pain processing. Evidence suggests the presence of central sensitization, which amplifies pain perception and contributes to its persistence [4, 5].

In addition to pain, deficits in the neuromuscular system also play an important role. Reduced muscle strength, particularly when combined with impaired proprioception, has been shown to significantly contribute to activity limitations, indicating that motor control deficits are central to disability in this population [6]. Structural factors may further compound these functional impairments, as decreases in bone and muscle parameters, including lower cortical bone mineral content, small cortices, and lower muscle mass, have been observed [7], potentially affecting load-bearing capacity and increasing vulnerability to injury.

Fatigue is another highly prevalent and disabling symptom, often occurring alongside autonomic dysfunction. Orthostatic intolerance has been identified as a significant contributor to fatigue severity, limiting tolerance to prolonged standing and physical exertion [8]. Additional factors associated with greater fatigue include physical activity participation, higher self-perceived extent of joint hypermobility, and reduced social functioning [9]. Moreover, emerging evidence indicates that altered muscle–tendon mechanics may increase the metabolic cost of movement, thereby reducing exercise efficiency and contributing to early fatigue during physical activity [10].

Respiratory symptoms also play a role in limiting physical capacity. Patients frequently report dyspnea and reduced exercise tolerance, which may be partially explained by mechanical ventilatory constraints, manifested by a decrease in inspiratory capacity and increase in the end expiratory lung volume, observed during exertion [11]. These findings are supported by broader observations of respiratory manifestations in this population, which have both physical and psychosocial consequences, including pain exacerbation, reduced exercise capacity, dyspnea, anxiety, depression, sleep disturbances, and impaired social functioning [12].

3.2. Psychological factors and physical activity patterns

The substantial physical burden experienced by individuals with hEDS/HSD is closely intertwined with psychological factors, which further influence disease presentation and functional outcomes. A growing body of evidence indicates a higher prevalence of psychiatric comorbidities, including anxiety, depression, and obsessive-compulsive disorder. Furthermore, individuals with hEDS have been reported to show higher rates of tobacco and alcohol use[13]. These psychiatric and behavioural conditions are often linked to chronic pain, diagnostic uncertainty, and long-term functional limitations, creating a bidirectional relationship between psychological distress and physical symptoms.

Existing research provides deeper insight into the psychosocial impact of the condition, describing significant disruptions in daily life, social participation, and self-identity. Patients frequently report feelings of frustration, lack of validation, and difficulties in maintaining employment or education [14, 15]. Chronic pain, in particular, is associated with cognitive and emotional challenges, including catastrophizing, hypervigilance, and reduced coping capacity [16].

These psychological factors strongly influence attitudes toward physical activity. Individuals with hEDS/HSD often hold varied beliefs about exercise, including uncertainty regarding its role in pain management and long-term condition control. Although many patients recognize the general health benefits of physical activity, fewer perceive it as effective in alleviating pain. Beliefs about the importance of exercise for long-term management and wellbeing, combined with guidance from healthcare professionals, appear to significantly influence exercise behaviour in this population [17].

Studies suggest that adolescents with hEDS/HSD present reduced levels of moderate-to-vigorous physical activity, increased sedentary time, and overall activity profiles associated with poorer health compared to healthy peers [18]. These findings are particularly concerning

given the potential long-term consequences of physical inactivity in a population already burdened by pain, fatigue, and functional limitations.

3.3. Effects of exercise and rehabilitation in hEDS/HSD

Exercise and rehabilitation interventions constitute a central component of management strategies in individuals with hEDS/HSD, although the evidence base remains heterogeneous in both quality and outcomes. Systematic and scoping reviews generally indicate that structured physical therapy can lead to improvements in pain, physical function, and quality of life; however, the strength of evidence is limited by small sample sizes and methodological variability [19, 20].

Resistance training, in particular, has been proposed as both feasible and potentially effective in this population, with potential benefits related to improved muscle function and joint stabilization. Most intervention programmes have incorporated closed kinetic chain exercises performed using body weight, resistance bands, or balance boards to provide resistance and proprioceptive challenge. Such interventions have been associated with reductions in pain, improvements in muscular strength and joint stabilization, as well as enhanced performance of activities of daily living (ADLs) [21].

These findings are supported by interventional studies demonstrating that targeted exercise programs can improve joint-specific outcomes. For example, home-based exercise therapy has been shown to significantly reduce shoulder instability and improve function in patients with hEDS/HSD [22]. Furthermore, systematic reviews of conservative interventions for shoulder symptoms report statistically significant reductions in the occurrence of joint instability episodes, as well as reductions in pain and improvements in functional outcomes, with interventions including exercise, kinesiology taping, and the use of an elasticized short-sleeve compression jacket [23].

Multidisciplinary rehabilitation approaches may further enhance these effects by addressing the complex and multifactorial nature of the condition. Programs integrating physical therapy, education, and behavioural strategies have demonstrated improvements in both physical and psychosocial outcomes, including functional disability, motor performance, muscle strength, perceived harmfulness, and pain intensity, particularly in adolescents with chronic musculoskeletal pain [24]. Similarly, prospective controlled studies indicate that structured rehabilitation programs can yield sustained benefits in functional exercise capacity and quality of life over both short- and medium-term follow-up periods, corresponding to 6 weeks and 6 months after the end of the rehabilitation program [25].

Emerging evidence suggests that alternative and more specialized exercise modalities may also provide beneficial outcomes. Neurocognitive and neuromodulatory exercise-based interventions have shown moderate evidence of effectiveness in reducing chronic pain, supporting the role of central nervous system mechanisms in rehabilitation [26]. Furthermore, preliminary studies suggest that even higher-intensity training protocols, including functional power training (FPT) and high-intensity interval training (HIIT) performed three times per week over 12 weeks, may be both feasible and safe in selected populations, including children with heritable connective tissue disorders [27], thereby challenging traditional assumptions that such individuals should avoid more demanding physical activity.

However, not all interventions provide consistent benefits. Evidence regarding the effectiveness of physical and mechanical therapies for lower limb symptoms, particularly in pediatric populations, remains inconclusive, with some studies reporting minimal or no significant effects [28].

Importantly, the question of safety remains central to the implementation of exercise interventions in this population. While current evidence generally supports the safety of well-designed and supervised exercise programs, there is still a lack of comprehensive synthesis addressing both risks and benefits across different intervention types. Ongoing research efforts aim to address this gap by systematically evaluating the safety and impact of physical activity in individuals with hEDS/HSD [29].

3.4. Risk associated with physical activity and sports participation

The relationship between joint hypermobility and injury risk during physical activity and sports participation remains complex and, in part, inconsistent across the literature. Several studies suggest that generalized joint hypermobility may predispose individuals to an increased risk of musculoskeletal injuries, particularly in high-demand athletic contexts. For instance, cohort data from elite-level soccer players indicate a higher incidence of injuries among hypermobile athletes [30], supporting the notion that joint laxity may compromise stability under dynamic loading conditions. Similarly, in a study of European female football players, generalized joint laxity was identified as a significant risk factor for sustaining an injury during both match play and training [31]. More recently, a study involving high school and college-aged competitive swimmers reported that hypermobility was associated with an increased risk of lumbar spine injuries [32].

Further evidence is provided by systematic review data demonstrating that generalized joint hypermobility is linked to an elevated risk of unilateral anterior cruciate ligament (ACL)

injuries in men, as well as poorer outcomes following ACL reconstruction [33]. These findings point not only to a higher likelihood of injury but also to more challenging recovery trajectories in hypermobile individuals.

However, not all findings are unequivocal. Broader analyses of hypermobility and sports injury highlight substantial heterogeneity in the results. In artistic gymnastics, where extreme ranges of motion are frequently required, higher levels of hypermobility were not associated with increased injury rates [34]. Similarly, a study comparing hypermobile and non-hypermobile lacrosse athletes found no significant differences in overall injury rates between the two groups [35]. Notably, one study reported a significantly higher incidence of joint and ligament sprains in the non-hypermobile group compared with the hypermobile group [36]. This inconsistency may reflect differences in study populations, types of sport, injury definitions, and degrees of hypermobility, suggesting that injury risk is likely context-dependent rather than universal.

4. Discussion

This narrative review underscores that the role of physical activity in individuals with hypermobile Ehlers–Danlos syndrome (hEDS) and hypermobility spectrum disorders (HSD) is complex, multifactorial, and highly individualized. The available evidence indicates that physical activity should not be viewed through a binary lens of benefit versus harm; rather, its effects depend on the interaction between underlying pathophysiology, psychological factors, and the characteristics of the activity itself.

The substantial physical burden observed in this population, including chronic pain, fatigue, neuromuscular deficits, and reduced exercise tolerance, provides an important context for interpreting physical activity behaviours. Chronic pain, often associated with central sensitization, contributes not only to symptom persistence but also to functional limitation [4,5]. At the same time, reduced muscle strength and impaired proprioception further compromise joint stability and motor control [6], while altered muscle–tendon mechanics may increase the metabolic cost of movement and contribute to early fatigue [10]. These findings collectively suggest that exercise intolerance in hEDS/HSD is not solely due to joint laxity but reflects broader systemic dysfunction.

Psychological factors further modulate these physical limitations. The increased prevalence of anxiety and depression [13], along with maladaptive cognitive responses such as catastrophizing and hypervigilance [16], plays a critical role in shaping attitudes toward movement. This is reflected in reduced participation in moderate-to-vigorous physical activity

and increased sedentary time in younger populations with hEDS/HSD [18]. Consequently, a self-reinforcing cycle may develop, in which pain and fatigue reduce activity levels, and inactivity in turn worsens physical capacity, psychological distress, and functional outcomes.

Despite these challenges, the overall body of evidence supports the role of exercise and rehabilitation as beneficial when appropriately prescribed. Systematic and scoping reviews consistently report improvements in pain, function, and quality of life following structured interventions, although the strength of evidence is limited [19, 20]. Resistance training appears particularly promising, contributing to improved muscle function and joint stabilization [21], while targeted interventions have demonstrated effectiveness in reducing joint-specific symptoms, such as shoulder instability [22, 23]. Moreover, multidisciplinary approaches integrating physical therapy, education, and behavioural strategies show enhanced outcomes, particularly in adolescents with chronic pain [24].

Emerging rehabilitation strategies further expand the therapeutic landscape. Neurocognitive therapeutic exercise-based interventions highlight the role of central mechanisms in pain modulation [26]. Additionally, evidence suggests that higher-intensity training may be both feasible and safe in selected populations [27]. Together, these findings challenge traditional conservative beliefs that often emphasize activity restriction, suggesting instead that overly cautious approaches may contribute to deconditioning and poorer long-term outcomes.

Nevertheless, the heterogeneity of available studies remains a significant limitation. Variability in study design, small sample sizes, and inconsistent outcome measures reduce the generalizability of findings. In particular, evidence regarding certain interventions, such as those targeting lower limb symptoms, remains inconclusive [28], highlighting the need for more robust research.

The question of injury risk further complicates clinical decision-making. While several studies report increased injury incidence in specific sports such as football, swimming, or in relation to ligamentous injuries, including ACL tears [30-33], other studies show no increased risk or even paradoxically lower injury rates in hypermobile athletes in certain disciplines [34-36]. These discrepancies likely reflect substantial heterogeneity in study design, definitions of hypermobility, sport-specific biomechanical demands, and participant characteristics. Therefore, injury risk should not be interpreted as a uniform consequence of hypermobility, but rather as context-dependent and modifiable.

Overall, the available evidence suggests that the key challenge is not whether physical activity is beneficial or harmful for individuals with hEDS/HSD, but rather how it is prescribed and implemented. Poorly adapted or unsupervised activity may exacerbate symptoms or increase

injury risk, whereas carefully tailored, progressive, and multidisciplinary exercise interventions can improve both physical and psychological outcomes. This reinforces the importance of individualized rehabilitation strategies that account for pain sensitivity, joint instability, fatigue, and psychological readiness, rather than applying generic exercise recommendations. Nevertheless, the considerable heterogeneity of exercise protocols, intervention duration, outcome measures, and study populations limits direct comparisons between studies and hinders the development of evidence-based clinical recommendations. Future research should prioritize high-quality, adequately powered trials using standardized intervention protocols and outcome measures to identify the most effective exercise strategies for different patient populations. Particular attention should also be given to the long-term effects of exercise interventions and their impact on overall physical function, quality of life, and participation in daily activities.

5. Conclusions

Physical activity in individuals with hEDS and HSD cannot be classified as universally protective or harmful. Instead, its impact is highly dependent on individual clinical presentation, exercise design, and supervision.

The available evidence indicates that while inherent physiological and biomechanical vulnerabilities may increase susceptibility to pain, fatigue, and certain injuries, appropriately prescribed exercise can improve muscle function, joint stability, pain levels, and overall quality of life. Psychological factors and behavioural patterns play a crucial role in shaping activity levels and should be addressed alongside physical rehabilitation.

Importantly, the current literature increasingly supports carefully individualized, structured, and multidisciplinary exercise approaches rather than unnecessarily limiting physical activity participation in individuals with hEDS/HSD. However, significant heterogeneity in study designs and limited high-quality evidence underline the need for further research to define optimal training parameters and long-term safety profiles in this population.

Disclosure

Author Contributions

Conceptualization: Zofia Golińska

Methodology: Zofia Golińska, Maciej Tomasz Zając

Software: Not applicable.

Check: Jakub Polczyk, Julia Rurkowska, Przemyslaw Rajzer
Formal analysis: Przemyslaw Rajzer, Wojciech Deptuch, Filip Maciej Ogorzałek
Investigation: Wiktor Szczuciński, Krzysztof Drelich, Wojciech Deptuch,
Resources: Filip Maciej Ogorzałek, Julia Rurkowska, Wiktor Szczuciński
Data curation: Paweł Krzysztof Moćko, Krzysztof Drelich, Przemyslaw Rajzer
Writing - original draft: Zofia Golińska, Maciej Tomasz Zając
Writing - review and editing: Maciej Tomasz Zając, Julia Rurkowska, Paweł Krzysztof Moćko, Wiktor Szczuciński
Visualisation: Krzysztof Drelich, Jakub Polczyk, Filip Maciej Ogorzałek
Supervision: Jakub Polczyk, Wojciech Deptuch, Paweł Krzysztof Moćko
Project administration: Zofia Golińska
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