

UPDATE ON THE DIAGNOSTIC CRITERIA FOR HEDS, THE DEFINITION OF HSD, AND EDS DIAGNOSTIC PATHWAY WORK



The Ehlers-Danlos Society has been supporting work on updating the 2017 diagnostic criteria for hypermobile Ehlers-Danlos syndrome (hEDS), improving the definitions of hypermobility spectrum disorders (HSD), and evidence-based diagnostic pathways.

The work on the criteria is being done by the hEDS/HSD and Pediatric Working Groups of The International Consortium on the Ehlers-Danlos Syndromes (EDS) and hypermobility spectrum disorders (HSD). The Society's role has been to facilitate the bringing together of members of these groups to work on the development of new criteria for children and young people and a review and development of the current criteria for adults.

The Society is also collaborating with members of the European Reference Networks (ERNs) on Rare and Uncommon Diseases to develop and publish evidence-based diagnostic pathways for all types of EDS.

The following is an update on this work and the next steps.

The review of hEDS Criteria and definition of HSD

The hEDS/HSD Working Group of the International Consortium met in 2019-20 and considered concerns that have been raised by the community and clinicians with regard to the

2017 criteria for hEDS. The group agreed that the criteria were conceived through a research lens to help improve research, progression, and understanding into the condition, and that review must consider, and determine through further study, the evidence that might lead to a broadening of the content of the criteria and changes to the structure of the criteria. They also reviewed the need for formal criteria for HSD. Formal studies, audits of clinical practice, and clinician and patient surveys (including those gathered for the 2018 scientific meeting in Ghent, Belgium) were considered to identify themes for further exploration.

Several key areas were identified for further exploration. These include:

- identifying additional methods for assessing the presence of generalized joint hypermobility (GJH) to assist in helping clinicians identify GJH;
- determining if the signs and complications considered typical of hEDS or HSD are sufficiently described in the current criteria;
- identifying which additional signs and complications should be added to support clinical assessment;
- working out whether all signs should remain equal to each other in the criteria, or whether certain signs were more significant than others i.e., carry more diagnostic weight;
- determining if there is now sufficient evidence to incorporate other signs and symptoms related to associated conditions/comorbidities into the criteria. Either way, the comorbidities should be ‘flagged’ at the end of the criteria as conditions to also consider;
- identifying which specific adjustments need to be made to the criteria so that they are appropriate for children and younger people; and,
- exploring concerns that have been raised surrounding the naming of hEDS, HSD.

The preparatory work for a study has been completed. This included a full review of the literature up to Dec 2020 and the development of a study protocol to explore whether, and to what degree, different signs and symptoms separate people with hEDS from people with HSD, and people with hEDS or HSD from other causes of widespread chronic pain. The study will include children and young people as well as adults.

The study protocol is currently under IRB review. As soon as it is approved it will be possible to start this study internationally. Please note that participants will be recruited from patients with chronic widespread musculoskeletal pain attending specialist clinics for expert evaluation through study sites as part of those sites’ normal clinical practice.

It is likely the study will take 12-18 months to complete. Once complete the data, including the diagnostic criteria model(s) that show the most sensitivity and specificity in identifying hEDS and HSD compared to other causes of chronic pain will be shared with stakeholders and discussed before publishing any recommendations if the research identifies that an update of the 2017 criteria is needed.

Development of the hEDS and HSD criteria for children and adolescents

Members of the Pediatric Working Group also sit on the hEDS/HSD Working Group and have been involved in the plans described above.

The Pediatric Working Group recognizes that the 2017 criteria, which were developed with the older adolescent and adults in mind, are difficult to use for children before they are fully grown. And, that this is creating issues for both families and health professionals.

The Working Group has prioritized developing a set of diagnostic criteria for children, with contributions from experts who are familiar with using the current tools in clinical practice in this age group.

The aim is to publish a framework based on expert consensus by the end of 2021 to fill this gap and then to develop an evidence base for the framework with adjustments as necessary, over the next couple of years.

Guidelines for the Diagnosis of all types of Ehlers-Danlos Syndrome

Towards the end of 2019 a group of experts, including representatives of The Ehlers-Danlos Society, The International Consortium on Ehlers-Danlos syndromes and hypermobility spectrum disorders, selected European Reference Networks on Rare and Uncommon Diseases (ReCONNET, VASCERN, and ERN SKIN), and patients' associations, met to reach a consensus on developing guidelines for the diagnosis of Ehlers-Danlos syndromes (EDS).

The following aims of diagnostic guidelines were identified:

- The guidelines should be targeted at a global audience, with the understanding that specific pathways may need to be developed in different regions to work within the local healthcare set up.
- These guidelines should help generalists who are not familiar with EDS in identifying likely cases of EDS for specialist evaluation.
- These guidelines should also help generalists and specialists who are not familiar with Medical Genetics in sending the 'right' patients to Medical Genetics Services with experience in the field of EDS/hereditary connective tissue disorders.
- At the same time, the guidelines would help Medical Geneticists (i) to select patients for molecular testing, (ii) to identify the most effective laboratory diagnostic workflow for the specific clinical suspicion, and (iii) to attribute the clearest clinical interpretation to the molecular results.
- The guidelines should be developed using a best-practice, evidenced-based approach.
- The guideline panel should include representatives from the involved European Reference Networks who will join members of the International Consortium on Ehlers-Danlos syndromes and hypermobility spectrum disorders.

It has been agreed that this work will be coordinated through the Center for Medical Genetics, Ghent University and Ghent University Hospital, and will commence in 2021. The work is likely to take 12 months to complete.

Moving Forward

This is a considerable amount of work. The Ehlers-Danlos Society is truly grateful to the many people who have given their time to this, and for the support of donors in helping to make this happen.

The COVID-19 pandemic has led to inevitable delays, but we look forward to progressing this work over 2021, and providing updates as soon as we are able.

We understand how essential this work is, and we are committed to ensuring it is done in the most thorough, collaborative, and evidence-based way.

We are grateful for the community's patience whilst waiting for these important tools to improve diagnosis and quality of life for people with EDS and HSD.