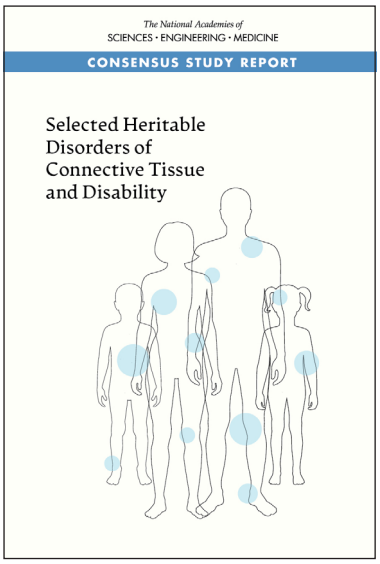
Consensus Study Report
HIGHLIGHTS
JUNE 2022

Selected Heritable Disorders of Connective Tissue and Disability



Heritable disorders of connective tissue (HDCTs) are a diverse group of inherited (genetic) disorders and subtypes. Because connective tissue is found throughout the body, HDCTs manifest in multiple body systems. The symptoms and physical and mental impairments associated with HDCTs vary widely and may develop and vary in severity (wax and wane) throughout an affected individual's lifetime. In some cases impairments associated with HDCTs may be severe enough to qualify an eligible child or adult for monetary benefits through the U.S. Social Security Administration's (SSA's) Social Security Disability Insurance or Supplemental Security Income program.

To examine the current state of medical knowledge and practice regarding selected HDCTs, SSA asked the National Academies of Sciences, Engineering, and Medicine to convene an expert committee that would provide current information regarding the diagnosis, treatment, and prognosis of selected HDCTs, including Marfan syndrome (MFS) and Ehlers-Danlos syndromes (EDS), and the effect of the disorders and their treatment on functioning. The resulting report, *Selected Heritable Disorders of Connective Tissue and Disability,* presents the committee's findings and conclusions.

HERITABLE DISORDERS OF CONNECTIVE TISSUE AND SSA DISABILITY

For eligible adults, SSA disability is defined as an "inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months." Eligible children under the age of 18 are considered disabled if they have "a medically determinable physical or mental impairment or combination of impairments that causes marked and severe functional limitations, and that can be expected to cause death or that has lasted or can be expected to last for a continuous period of not less than 12 months."

SSA disability determinations for children and adults follow a three-step and five-step sequential evaluation process, respectively. For both groups, SSA determines at step 3 whether the severity of the person's impairment(s) meets or medically equals the criteria listed for one of the conditions in SSA's Listing of Impairments-Adult Listings or Childhood Listings (listings). For children, SSA also considers whether the impairment(s) functionally equals the

criteria in the listings. Disability claims related to HDCTs are evaluated under listings for the affected body systems (e.g., musculoskeletal, neurological, gastrointestinal, etc.). With the exception of MFS, which is identified under one of the cardiovascular listings, HDCTs are not specified in the listings.

A challenge in the assessment of functioning in individuals with HDCTs is capturing the full effect of their impairment(s) on their daily activities, including participation in work and school. This is particularly true when a person has multiple impairments. Individuals with HDCTs may experience significant and unpredictable variability in their physical and/or mental secondary impairments from day to day or even within a single day.

SELECTION OF HERITABLE DISORDERS OF CONNECTIVE TISSUE

As directed in the committee's Statement of Task, the report focuses primarily on MFS and EDS because of their relative prevalence. MFS is an autosomal-dominant disorder that affects multiple organ systems, especially the ocular, cardiovascular, and skeletal systems. Thirteen types of EDS have been identified, all of which share common elements of joint hypermobility and skin and soft tissue involvement; hypermobile EDS (hEDS) is by far the most prevalent EDS type. In addition to MFS and EDS, the committee identified for inclusion in the report several other hereditary aortopathies (Loeys-Dietz syndrome, congenital contracture arachnodactyly [also known as Beals-Hecht syndrome], and Shprintzen-Goldberg syndrome) and hypermobility spectrum disorders because of the features they share with MFS and hEDS, respectively.

THE COMMITTEE'S OVERALL CONCLUSIONS

Based on its review of the relevant evidence, the committee formulated eight overall conclusions in seven areas: (1) nature of HDCTs, (2) HDCTs and disability, (3) diagnosis, (4) management, (5) barriers to access to care, (6) education, and (7) research gaps.

Nature of Heritable Disorders of Connective Tissue

1. HDCTs comprise a large and varied group of disorders in children and adults that share the common feature of pronounced involvement of connective tissues, usually in multiple organ systems. HDCTs can lead to a variety of physical and mental secondary impairments (i.e., manifestations, medical diagnoses, syndromes, comorbidities, or other health conditions) and associated functional limitations. Impairments can range from minor to severe and even life-threatening and may fluctuate in severity over time in an individual. Functional limitations may be sufficiently severe to interfere with participation in work and school, as well as social and recreational activities, and may include precautions and restrictions on activities to avoid aggravating the condition.

Heritable Disorders of Connective Tissue and Disability

2. Some of SSA's Adult Listings apply directly to secondary impairments experienced by individuals with HDCTs and could be used to evaluate disability in those individuals. Other listings, with some modification, could apply to certain secondary impairments experienced by individuals with HDCTs.

Diagnosis

3. Early diagnosis of HDCTs is important to reduce physical injury, reduce psychological harm to the individual and family members, and prevent the risks associated with inappropriate or fragmented medical care.

Management

4. Although curative treatments for HDCTs do not exist at this time, appropriate understanding and management of the disorders can reduce the frequency and severity of their manifestations and resulting functional consequences. High-quality care for individuals with HDCTs relies on effective coordination among a team of clinicians across a broad range of physical and mental health care disciplines who are knowledgeable about these disorders.

Barriers to Access to Care

5. Access to comprehensive, multidisciplinary care for the diagnosis and management of HDCTs can be limited by geography and other factors, including the availability of care teams with expertise in the disorders.

Education

6. Education about HDCTs, including their multisystem manifestations, diagnosis, and management, is important for all clinicians to help increase recognition and earlier diagnosis of the disorders and enable the provision of appropriate care.
7. Education of individuals with the disorders and their families, as well as employers and school staff, is important to improve the quality of life for affected individuals and their families, to facilitate appropriate accommodations at work and school, and to help inform the disability assessment and determination process.

Research Gaps

8. Ongoing research on HDCTs is important to advance understanding of the disorders and their effects. In particular, research on care services and interventions for HDCTs and secondary impairments is needed, including
    - more specific diagnostic criteria and biomarkers;
    - functional and biomeasures of severity;
    - effective treatment for HDCTs and management of their physical and mental manifestations, including comparative treatment trials;
    - the clinical course of the disorders throughout the lifetime of affected individuals;
    - the impact of relevant reasonable accommodations on affected individuals' ability to participate in work and school; and
    - benefits versus risks of participation in common childhood activities (e.g., contact sports, gymnastics, dance).

IN CONCLUSION

HDCTs are a large and varied group of disorders in children and adults that share the common feature of having a significant impact on connective tissues, usually in multiple organ systems. HDCTs can manifest in a variety of symptoms and physical and mental impairments, with associated functional limitations that may be sufficiently severe to interfere with participation in work and school. Although curative treatments for HDCTs do not exist at this time, early diagnosis, improved understanding, and appropriate management of the disorders can reduce the frequency and severity of their manifestations and resulting functional consequences. Health care providers in a variety of fields should receive education about HDCTs so they are able to recognize the disorders and direct affected individuals to the appropriate clinicians for management. It is important to note that even with proper treatment, some individuals may still experience significant limitations in functioning. Ongoing research on care services and interventions for HDCTs and the secondary impairments associated with them is needed.

For more detail on the committee's conclusions about diagnosis and education, please see the 1-page insert on overall conclusions.

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To read the full report, please visit
http://www.nationalacademies.org/connective-tissue-disorders