"Red Flags" suggesting the presence of a genetically defined type of Ehlers-Danlos Syndrome or other heritable disorder of connective tissue.

Table 2 General features, head and neck, and facial feature "red flags" suggesting the presence of a genetically determined type of EDS or related heritable disorder of connective tissue.

	c EDS	cl EDS	cv EDS	v EDS	a EDS	d EDS	k EDS	BCS	sp EDS	mc EDS	m EDS	p EDS	Marfan syndrome	Loeys–Dietz syndrome	Osteo-genesis imperfecta	Stickler syndrome
General																
Short stature						X			X						X	
Sudden, early unexpected death (under age of 40)													X	X		
Hernia (umbilical or inguinal)	X		X			X	X					X	X	X		
Acrogeria (prematurely aged appearance)				X								X				
Developmental delay (motor)											X					
Head, ENT, craniofacial																
Characteristic facial appearance				X		X	X		X	X		X	X	X	X	X
Epicanthal folds	X															
Keratoconus				X				X								
Clouded cornea									X							
Ocular fragility							X	X								
Dislocation of the ocular lens													X			
Retinal detachment								X								X
Deafness							X	X							X	X
Cleft palate or bifid uvula														X		X
Gingival recession and gingival fragility				X								X				
Severe periodontal disease												X				
Dentinogenesis imperfecta (teeth with thin enamel)															X (in some types)	

Abbreviations: *AD*, autosomal dominant; *aEDS*, arthrochalasia EDS; *AR*, autosomal recessive; *BCS*, Brittle Cornea Syndrome; *cEDS*, classical EDS; *dEDS*, classical-like EDS; *cvEDS*, cardiac-valvular EDS; *dEDS*, dermatosporaxis EDS; *kEDS*, kyphoscoliotic EDS; *mcEDS*, musculocontractural EDS; *mEDS*, myopathic EDS; *pEDS*, periodontal EDS; *spEDS*, spondylodysplastic EDS; *vEDS*, vascular EDS.
Credit: Authors' own work.

Table 3 Musculoskeletal and skin "red flags" suggesting the presence of a genetically determined type of EDS or related heritable disorder of connective tissue.

	c EDS	clEDS	cv EDS	v EDS	a EDS	d EDS	k EDS	BCS	sp EDS	mc EDS	m EDS	p EDS	Marfan syndrome	Loeys–Dietz syndrome	Osteo-genesis imperfecta	Stickler syndrome
Musculo-skeletal																
Club foot (talipes equinovarus)				X			X		X	X				X		
Congenital hip dislocation				X	X											
Scoliosis or kyphoscoliosis					X		X	X		X			X	X	X	
Muscle hypotonia					X		X	X	X		X					
Muscle weakness		X														
Hypermobility limited to distal joints				X				X			X					
Osteopenia or osteoporosis at a young age							X		X						X	
Osteoarthritis at a young age (<40)														X	X	X
Brachydactyly (short fingers and toes)		X														
Joint contractures								X	X	X	X			X		
Skin																
Extremely stretchy skin	X	X			X		X		X	X		X				
Extreme fragility	X					X	X									
Redundant skin						X										
Aged-appearing hands		X														
Increased palmar wrinkling (hands)						X				X						

Abbreviations: *AD*, autosomal dominant; *aEDS*, arthrochalasia EDS; *AR*, autosomal recessive; *BCS*, Brittle Cornea Syndrome; *cEDS*, classical EDS; *clEDS*, classical-like EDS; *cvEDS*, cardiac-valvular EDS; *dEDS*, dermatosporaxis EDS; *kEDS*, kyphoscoliotic EDS; *mcEDS*, musculocontractural EDS; *mEDS*, myopathic EDS; *pEDS*, periodontal EDS; *spEDS*, spondylodysplastic EDS; *vEDS*, vascular EDS.

Table 4 Other organ pathology "red flags" suggesting the presence of a genetically determined type of EDS or related heritable disorder of connective tissue.

	c EDS	clEDS	cv EDS	v EDS	a EDS	d EDS	k EDS	BCS	sp EDS	mc EDS	m EDS	p EDS	Marfan syndrome	Loeys–Dietz syndrome	Osteo-genesis imperfecta	Stickler syndrome
Cardio-vascular																
Severe progressive valvular heart disease			X													
Aortic or arterial aneurysms, dissection or rupture				X			X		X				X	X	X	
Pulmonary																
Pneumothorax				X						X			X			
Gastrointestinal																
Bowel rupture				X												
Colonic diverticula										X						
Genito-urinary																
Uterine rupture				X												
Bladder diverticula							X									

Abbreviations: *AD*, autosomal dominant; *aEDS*, arthrochalasia EDS; *AR*, autosomal recessive; *BCS*, Brittle Cornea Syndrome; *cEDS*, classical EDS; *clEDS*, classical-like EDS; *cvEDS*, cardiac-valvular EDS; *dEDS*, dermatosporaxis EDS; *kEDS*, kyphoscoliotic EDS; *mcEDS*, musculocontractural EDS; *mEDS*, myopathic EDS; *pEDS*, periodontal EDS; *spEDS*, spondylodysplastic EDS; *vEDS*, vascular EDS.
Credit: Authors' own work.

Source: Francomano CA, Hakim AJ, Henderson LGS and Henderson FC. Introduction: An overview of the Ehlers-Danlos syndromes and hypermobility spectrum disorders. *In* Francomano CA, Hakim AJ, Henderson GS, Henderson FC, eds. Symptomatic: The symptom-based handbook for Ehlers-Danlos Syndromes and Hypermobility Spectrum Disorders. Elsevier, Cambridge MA and Amsterdam, Netherlands. 2024