Generalized Joint hypermobility and Ehlers-Danlos syndromes:

an updated critique

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An introduction to generalized joint hypermobility and its syndromes

Joint

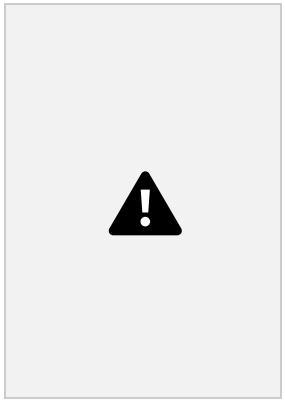
Joint hypermobility:

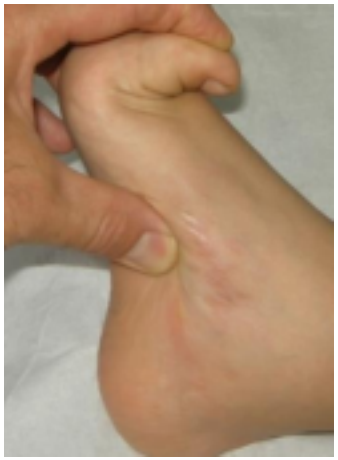
hypermobility

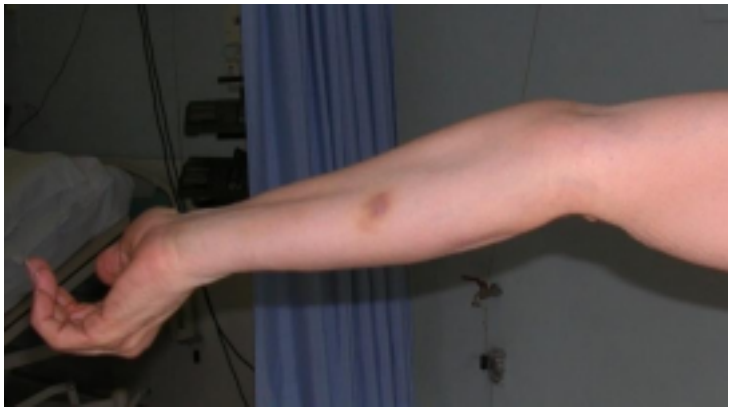
definitions

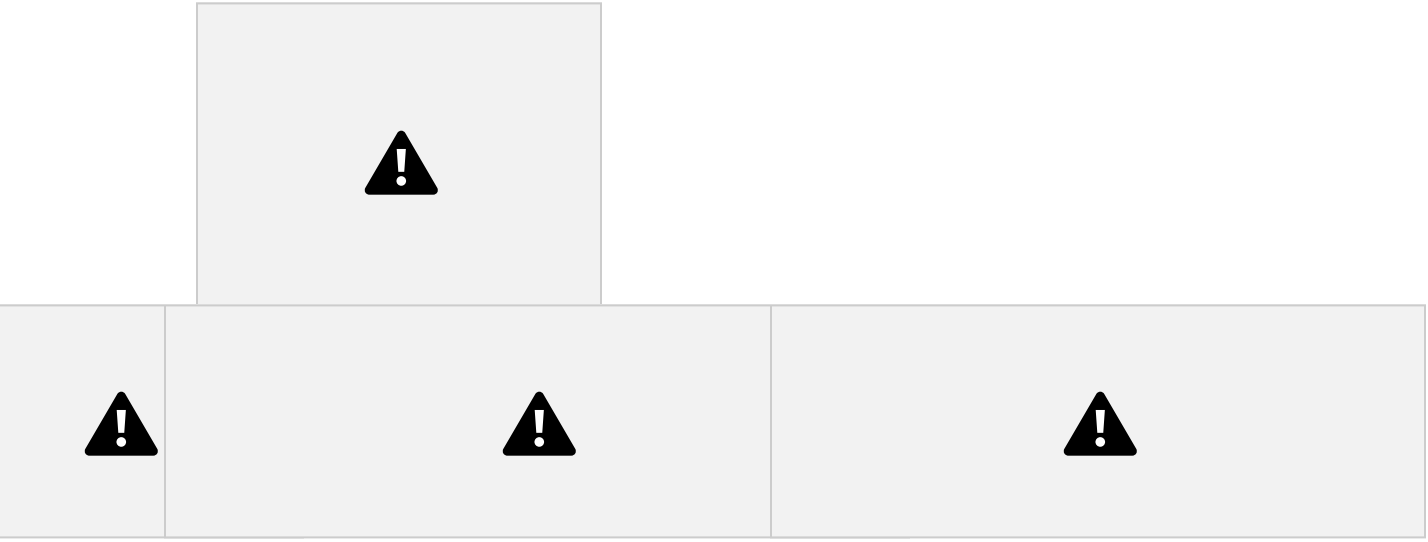
: definitions

Joint hypermobility (JHM): a joint or group of joints showing physiologic movement(s) beyond the limits usually accepted as "normal" (i.e. respecting ROM standards)







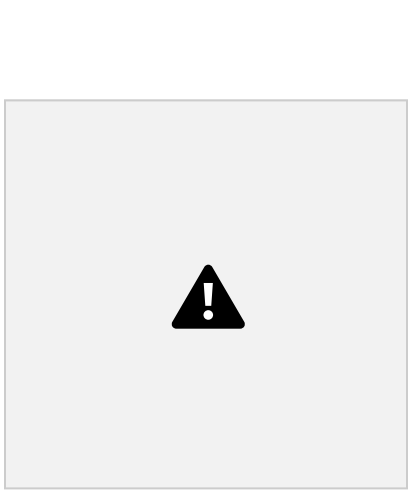
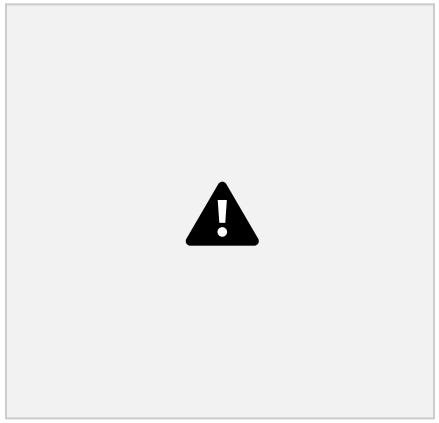
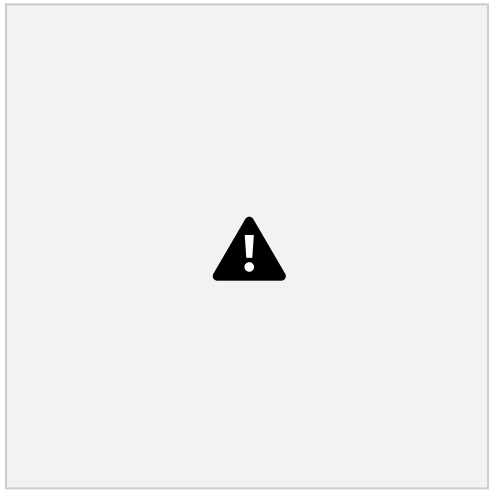
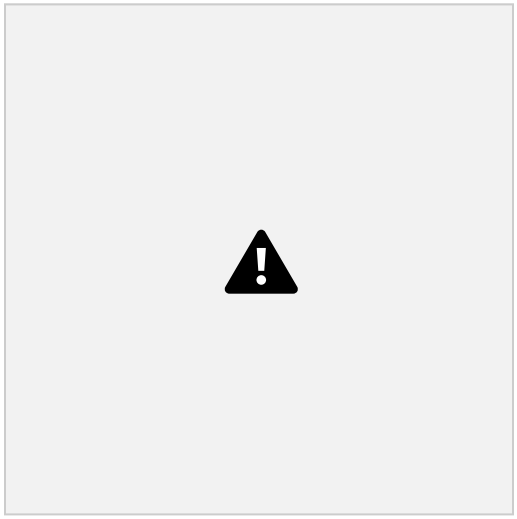
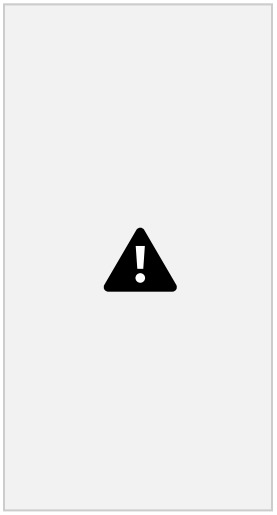
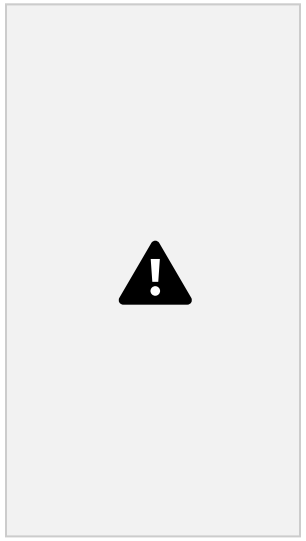


Joint hypermobility: definitions

Localized joint hypermobility: excessive motion of a *single* joint or group of joints

Peripheral joint hypermobility: *bilateral* joint hypermobility limited to *hands/feet*

Generalized joint hypermobility (gJHM): *widespread* joint hypermobility **Joint instability:** excessive joint mobility along physiological and/or *non physiological* axes (predisposing to dislocations)

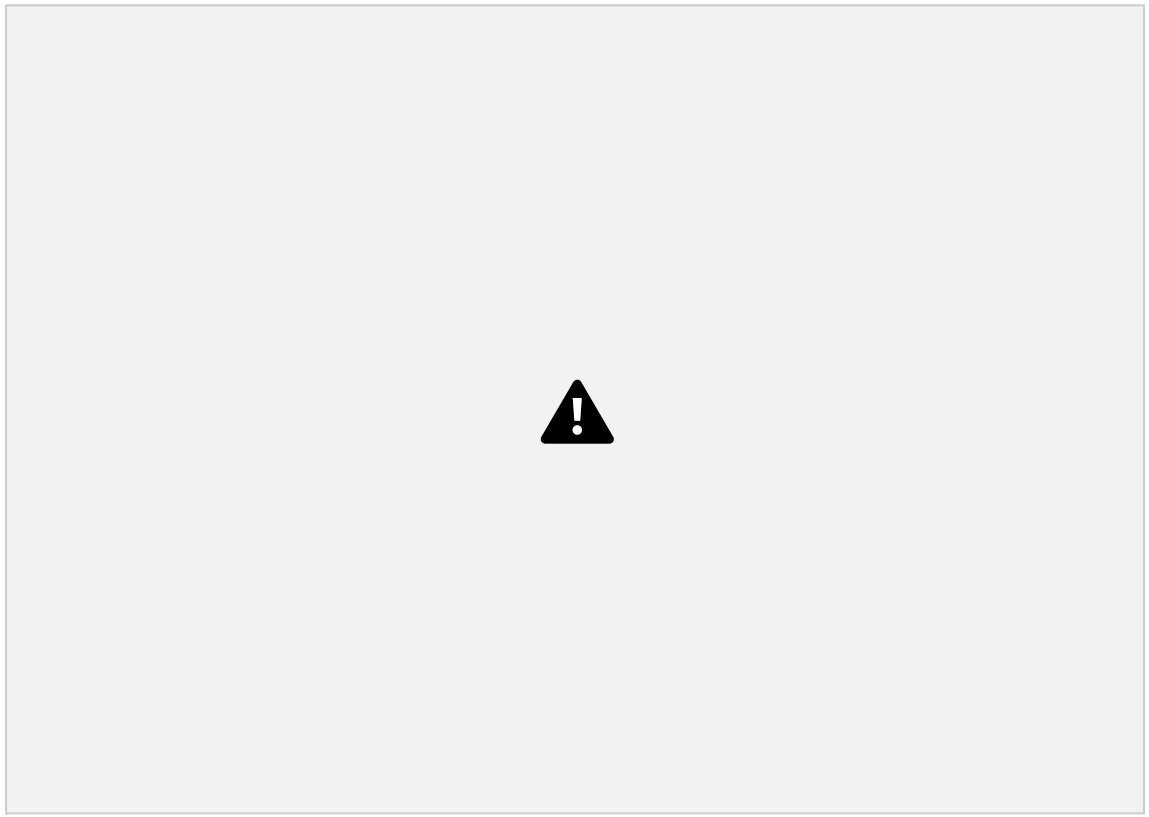







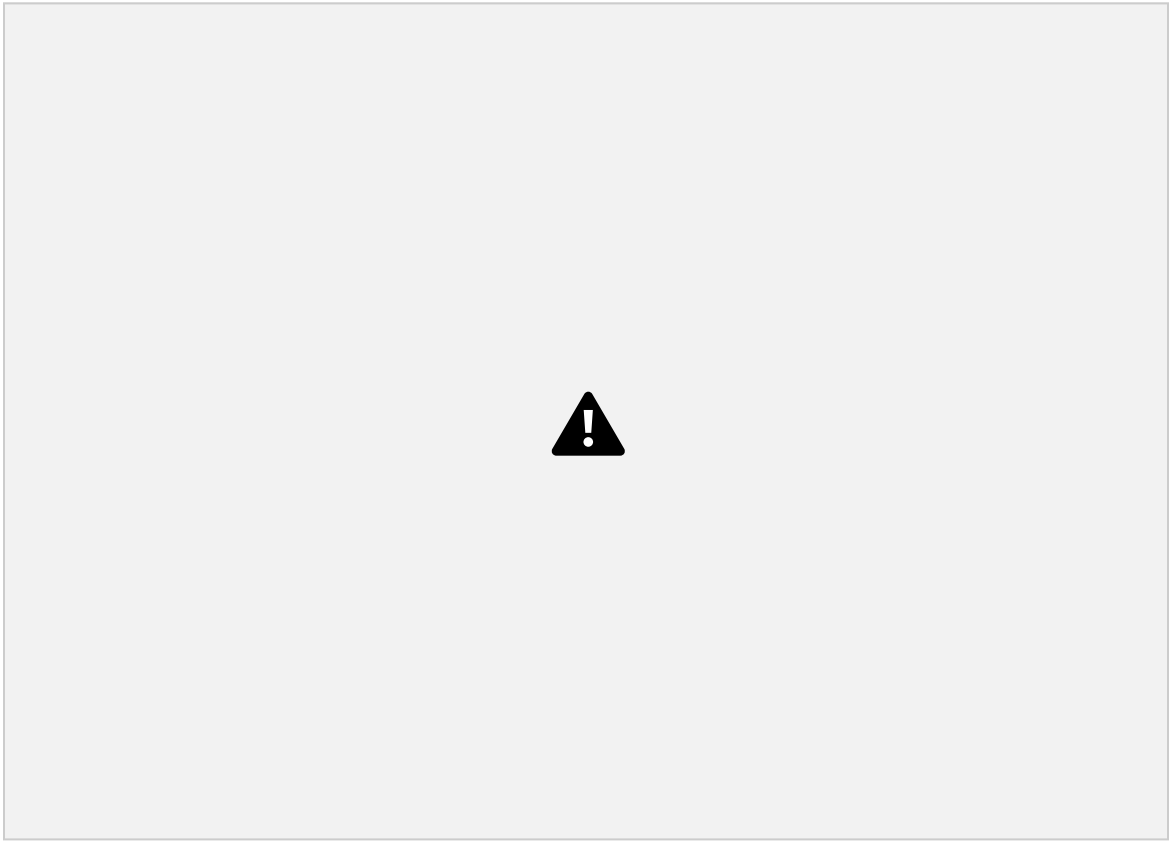
Localized

Peripheral Generalized


Joint

hypermobility: epidemiology





(Remvig et al., 2007)

JHM is well represented in all investigated populations, and is most common in children and females (Fs = 6-57%; Ms = 2-35%).

Limitations: heterogeneity of measurements, not clear distinction between JHM and gJHM, not clear distinction between non-sydromic and syndromic individuals.

Joint hypermobility: evaluation

LOCALIZED JOINT HYPERMOBILITY

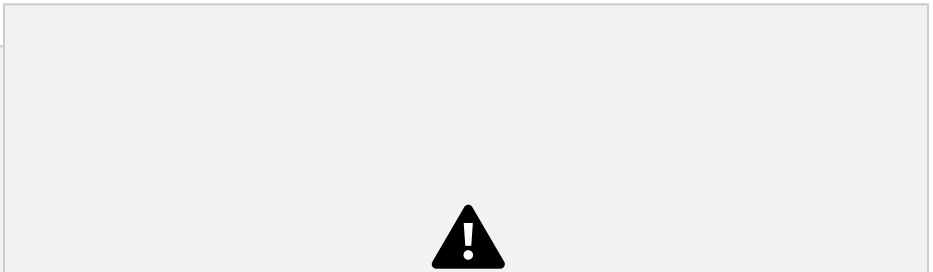
PERIPHERAL JOINT HYPERMOBILITY

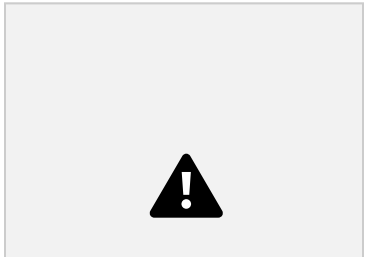
GENERALIZED JOINT HYPERMOBILITY

The suspect of a "systemic" disorder increases!

Measurement of

SINGLE JOINTS





JOINT HYPERMOBILITY GENERALIZED

Sex Age Ethnicity

Past surgeries/ traumas

Co-morbidities

Past habits (eg. sports)

ROMs Beighton score (BS)

Concurrentterapies

Hospital del mar score

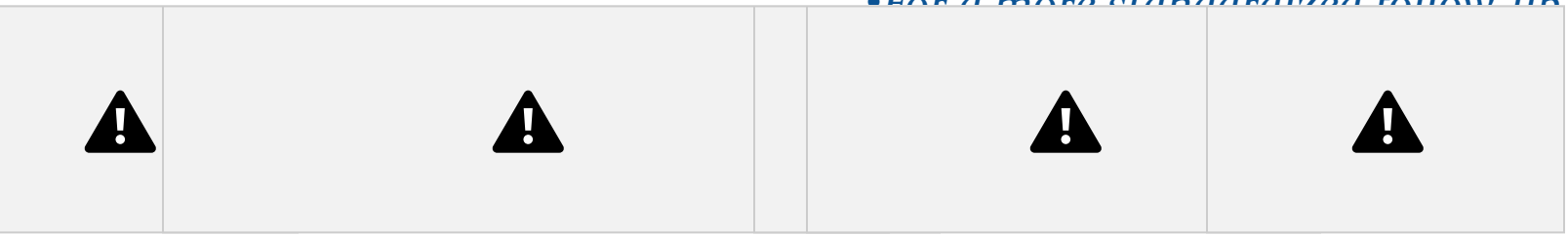


Joint hypermobility:

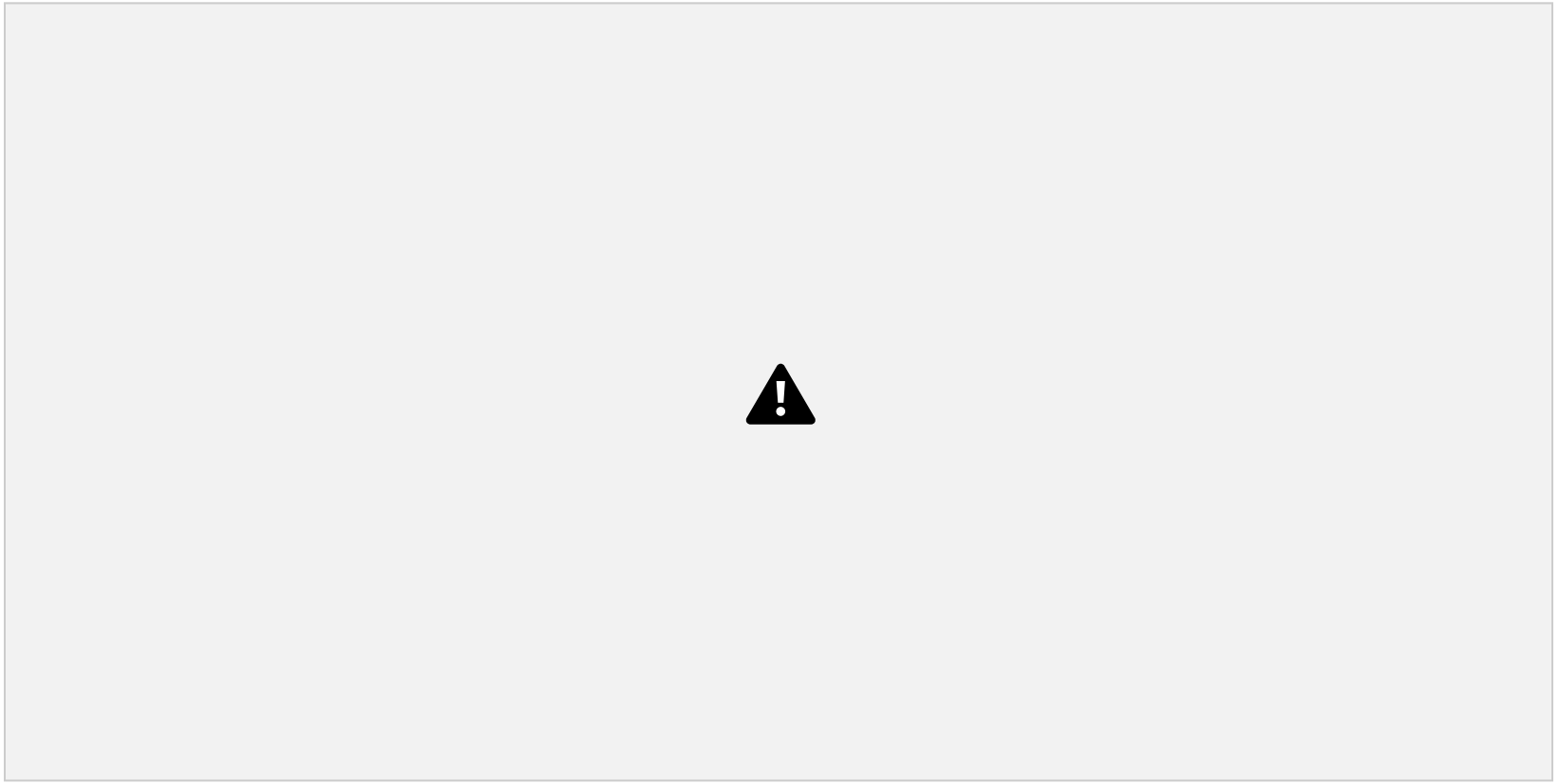
ROMs

ROMs should be measured by objective methods (e.g. orthopedic goniometer)

- *For minimizing the risk of FPs and FNs*
- *For a more standardized follow-up*

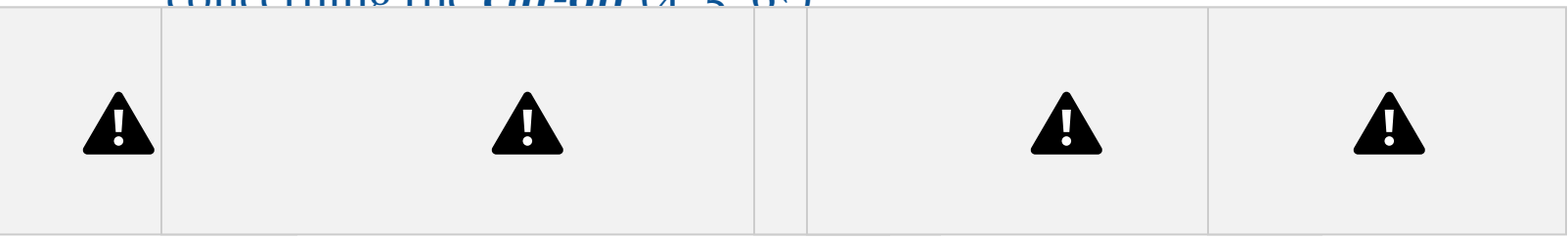


Joint hypermobility: Beighton score



(Voermans & Castori, 2014)

All tools assessing the presence of “generalized” JHM are **arbitrary** The Beighton score is the most commonly used method but debate exists concerning the ***cut-off*** (4, 5, 6?)



Joint

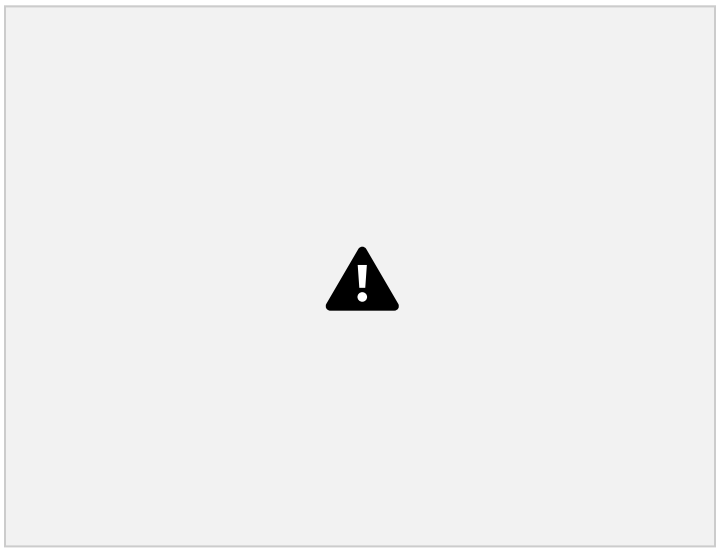
hypermobility: Beighton score

Villefranche criteria (for EDS-HT)	5	9
Brighton criteria (for JHS), major criterion	4	9
Brighton criteria (for JHS), minor criterion	1-3	9
Males	4	9
Children	6 or 7	9
Disabled or non collaborative subjects	NA	8
…	…	…

The Beighton score was originally identified as an epidemiological tool in African children (**Beighton et al., 1973**)

It was subsequently introduced in clinics without a formal validation

Joint hypermobility: syndromes…



Joint hypermobility:

syndr
omes
...

Clear-cut

✔ True global developmental delay

✔ Facial dysmorphism

✔ Pigmentary changes

✔ Abnormal growth pattern

Skeletal dysplasias
Chromosomal and genomic disorders

RASopathies

Generalized JHM distinguishing features:

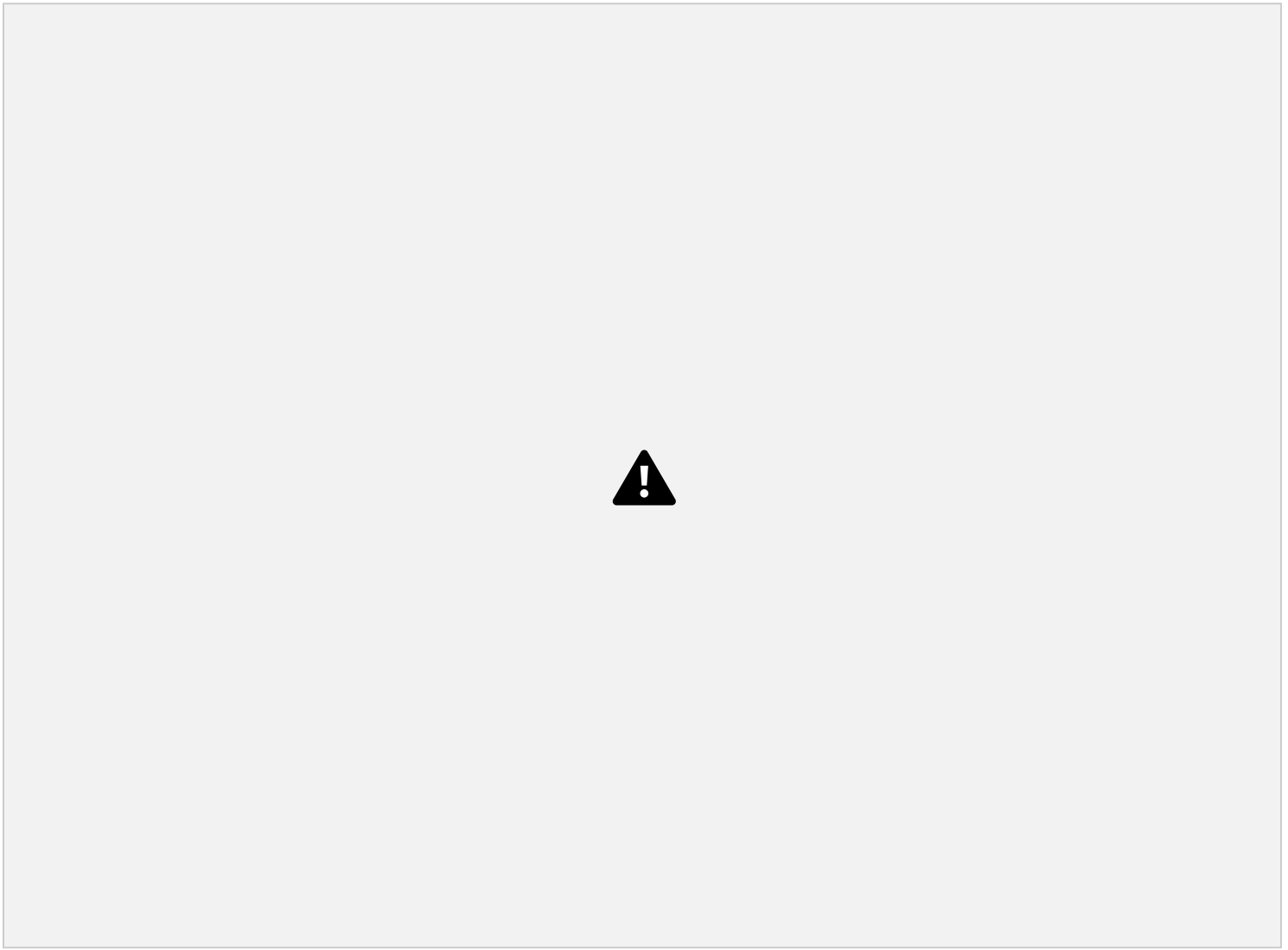
Systemic hereditary connective tissue disorders

syndromes

✔ ....

Rarer

Ehlers-Danlos Syndromes



(Castori, EOOD, in press)

Distinguishing among the EDSs

pathogenesis

Genotype-phenotype correlations

Different molecular defects

DISTINCTIVE FEATURES

Convergent

SHARED MANIFESTATIONS

Modular/organ-specific dysfunctions

Molecular splitting *versus* ***clinical lumping*** *in heritable soft connective tissue disorders*

Definiting Ehlers-Danlos syndrome, hypermobility type

EDS hypermobility type - 1969

EDS hypermobility type was first introduced as a common differential diagnosis of and an exclusion diagnosis from:

Classical EDS (mitis and gravis) – distinguisable for typical cutaneous involvement

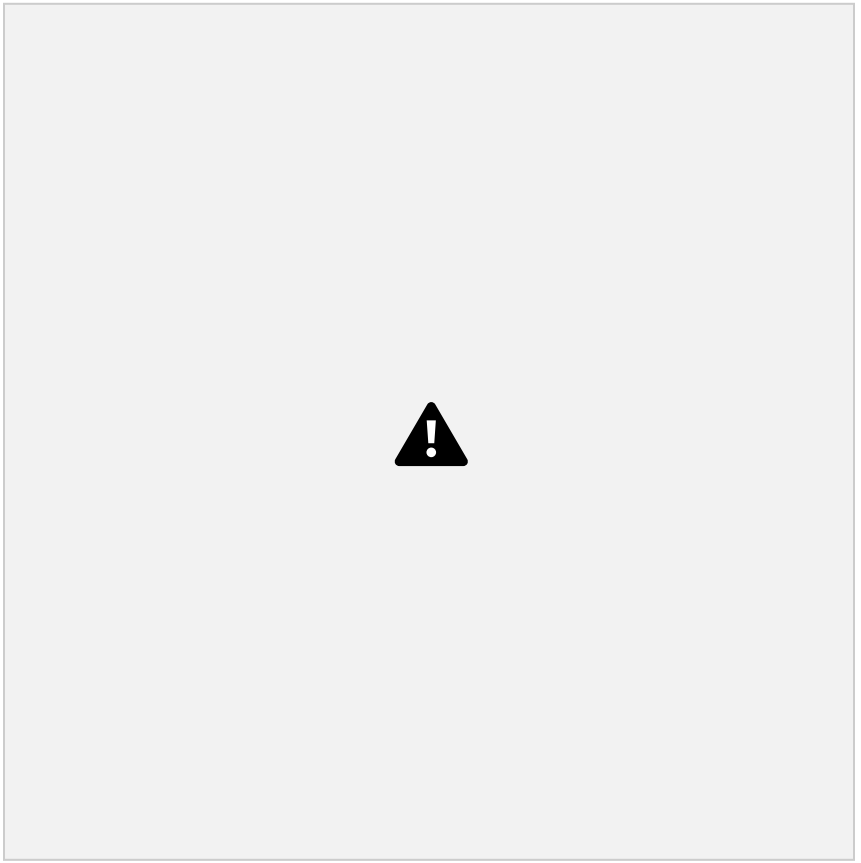
Vascular EDS – distinguishable for vascular features

gJHM as the most striking clinical sign

(Beighton et al., Ann Rheum Dis 1969)

EDS hypermobility type -

1973



Introduction of the **Beighton score** as an *epidemiological tool* for assessing for presence/absence of generalized joint hypermobility.

A tool first applied on African chidren

(Beighton et al., Ann Rheum Dis 1973)

Subsequently, considered a *clinical tool* in many populations…

(Remvig et al., J Rheumatol 2007)

… although with lack of consesus

(Remvig et al., Am j Med Genet A 2014)

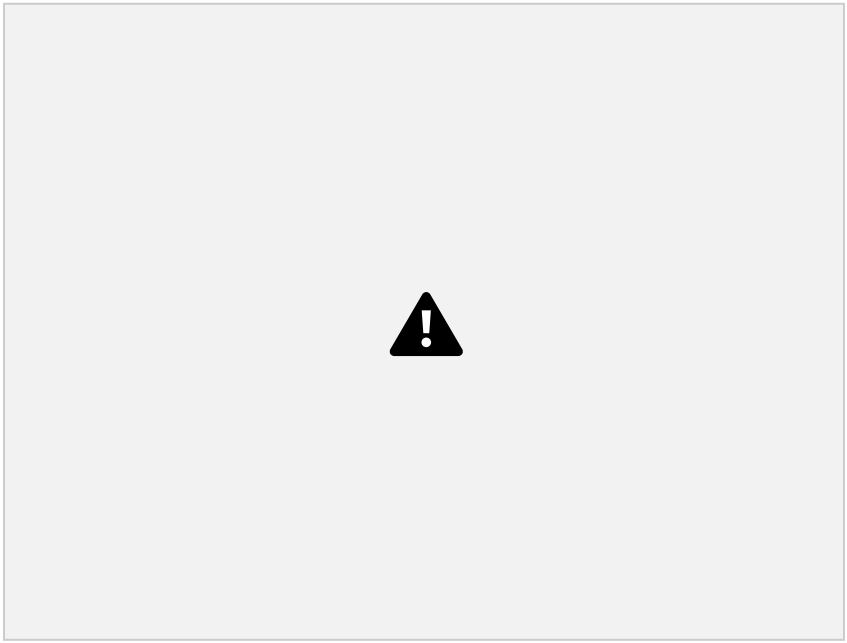
Limits of the Beighton score

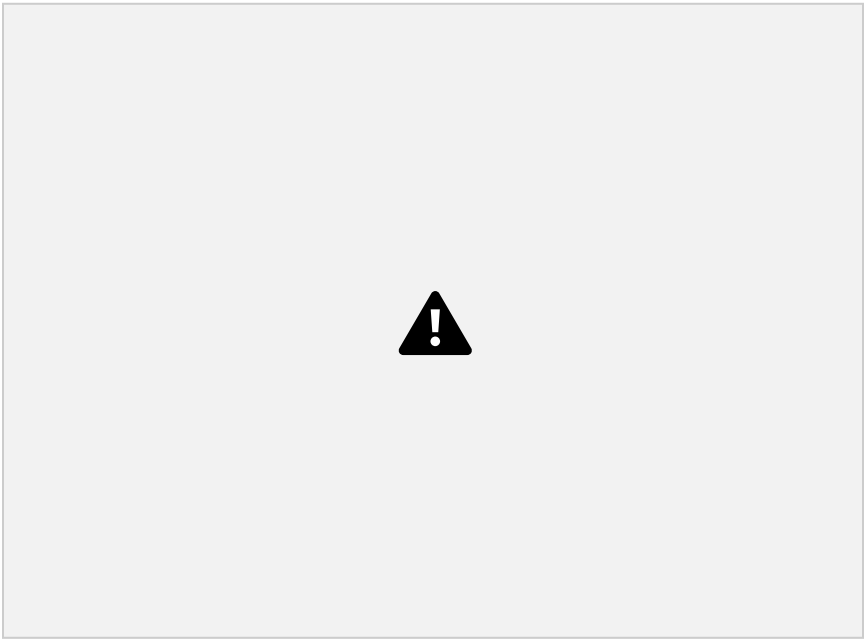
1. Reproducible but still high interindividual and intraindividual variability - *use of orthopedic goniometer and application of published recommendations not sufficiently emphasized*
2. Variability by age, sex and ethnic group - *modifiers not established*

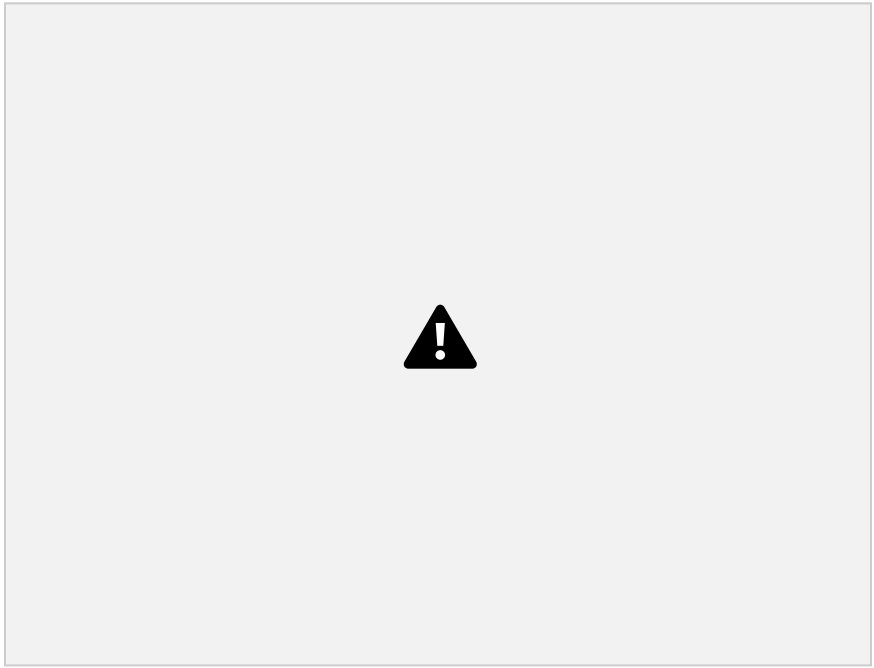
3. Limited number of considered joints – *circumstances for the use of complementary joints not defined*

4. Joint hypermobility not always corresponds to joint instability – *alternatives for measuring joint instability as a pathological manifestation of lax ligaments not included*

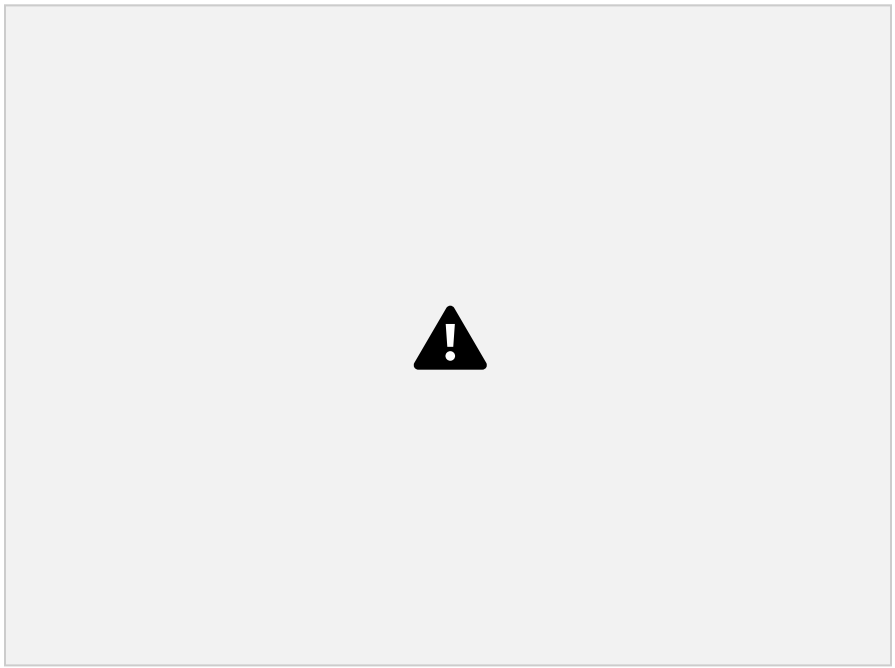
gJHM and age in EDS-HT







Natural reduction of the Beighton score in EDS-HT *(cross-sectional observation)*



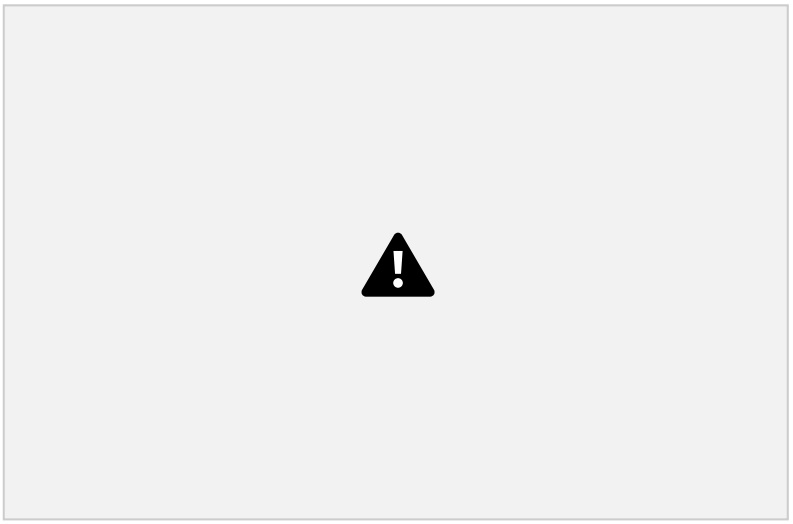
hypermobile joints outside the Beighton score in EDS-HT

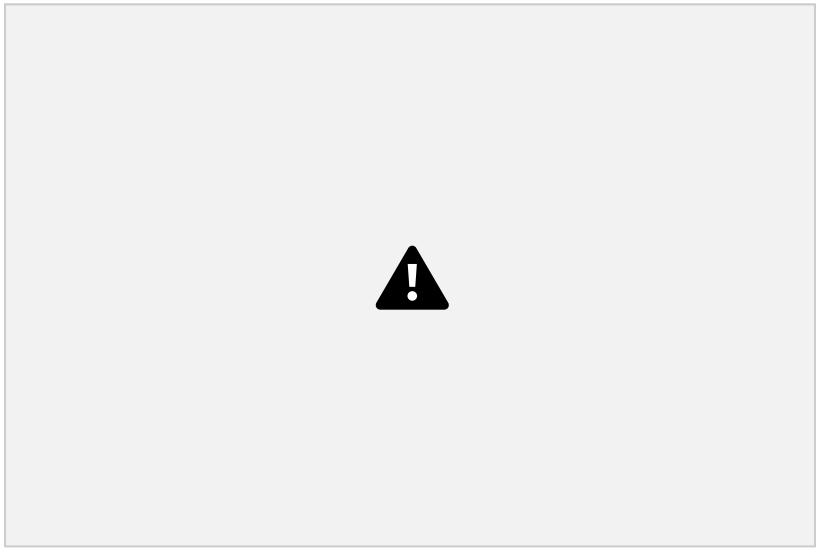
(cross-sectional observation)

Natural reduction of the number of

EDS hypermobility type -

1998





EDS hypermobility type is still a diagnosis of exclusion but based on relatively well-defined clinical diagnostic criteria

(Beighton et al., Am J Med Genet 1998)

Limits of the Villefranche criteria

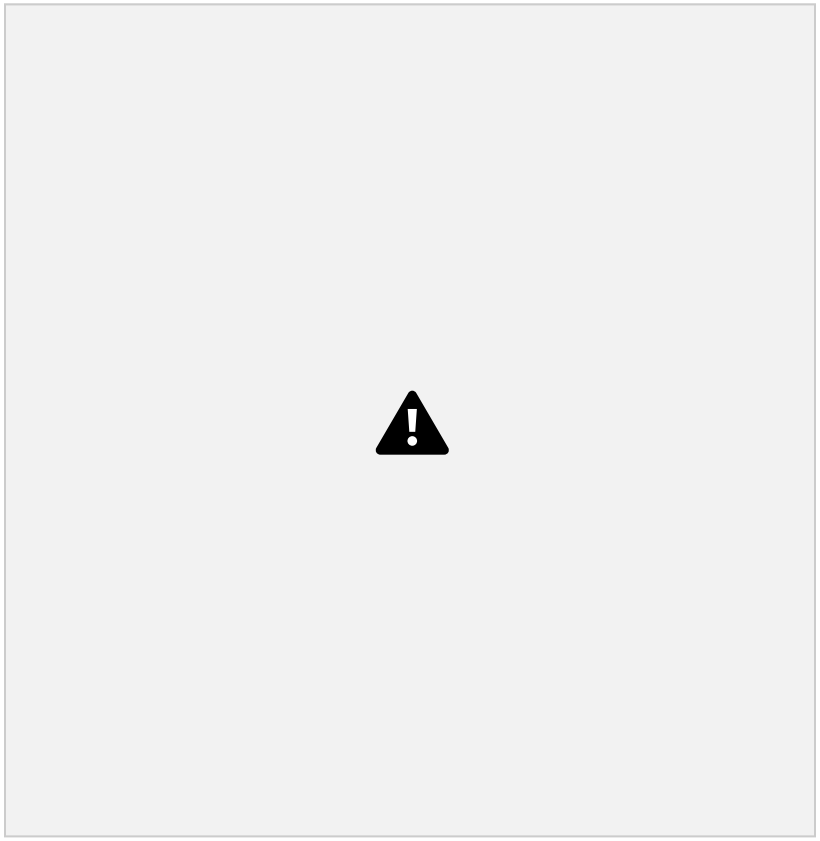
1. Limits of the Beighton score fully incorporated 2.

Skin sign, as a necessary feature, too loosely defined

3. Possibility of complete absence of symptoms (e.g. two major criteria only)

4. Possibility of overdiagnosis in children

EDS hypermobility type - 2000



Joint hypermobility syndrome first

introduced as *separate* from other syndromes with joint hypermobility

(Grahame et al., J Rheumatol 2000)

A closely complete clinical overlap with EDS-HT is proposed

(Tinkle et al., Am J Med Genet A 2009)

Not all researchers agree

(De Paepe and Malfait, Clin Genet 2012)

Co-segregation in *familial cases* is formally suggested

(Castori et al., Am J Med Genet A 2014)

Limits of the Brighton criteria

1. A lower Beighton score usually does not correspond to a past generalized joint hypermobility!
2. Possibility of diagnosis in the absence of objective generalized joint hypermobility and skin anomalies
3. Possibility of diagnosis on symptoms only (“symptomatic diagnosis”)
4. Likely overdiagnosis in adults

EDS hypermobility type - 2003




Presentation of the **5-point questionnaire** (5PQ) as a rapid screening tool for past/historical gJHM

(Hakim and Grahame, Int J Clin Pract 2003)

Useful for clinical orientation but it cannot be considered a substitute of physical examination

It cannot be considered a diagnostic criterion; hence it has a very limited clinical value to date.

EDS hypermobility type – 2009 to date





✔ Is still a clinical diagnosis without any confirmatory test

✔ The debate on the *clinical identity vs separation* between EDS-HT and JHS is far to be solved

✔ Many works, often with major limitations*, support the p*ossibility* of **poor QoL** for:

1. Chronic musculoskeletal **pain** and **physical disability**

2. Chronic **fatigue** and cardiovascular dysautonomia

3. Multiple **functional gastrointestinal disorders**

4. **Psychological distress**

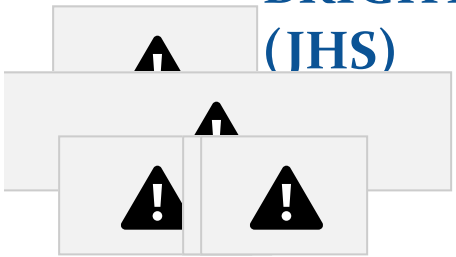
**: (1) Clustering with other EDS subtypes; (2) clustering with JHS without a critical approach to avaiable diagnostic criteria; (3) questionnaire studies without direct patients' examination; etc*

Brighton

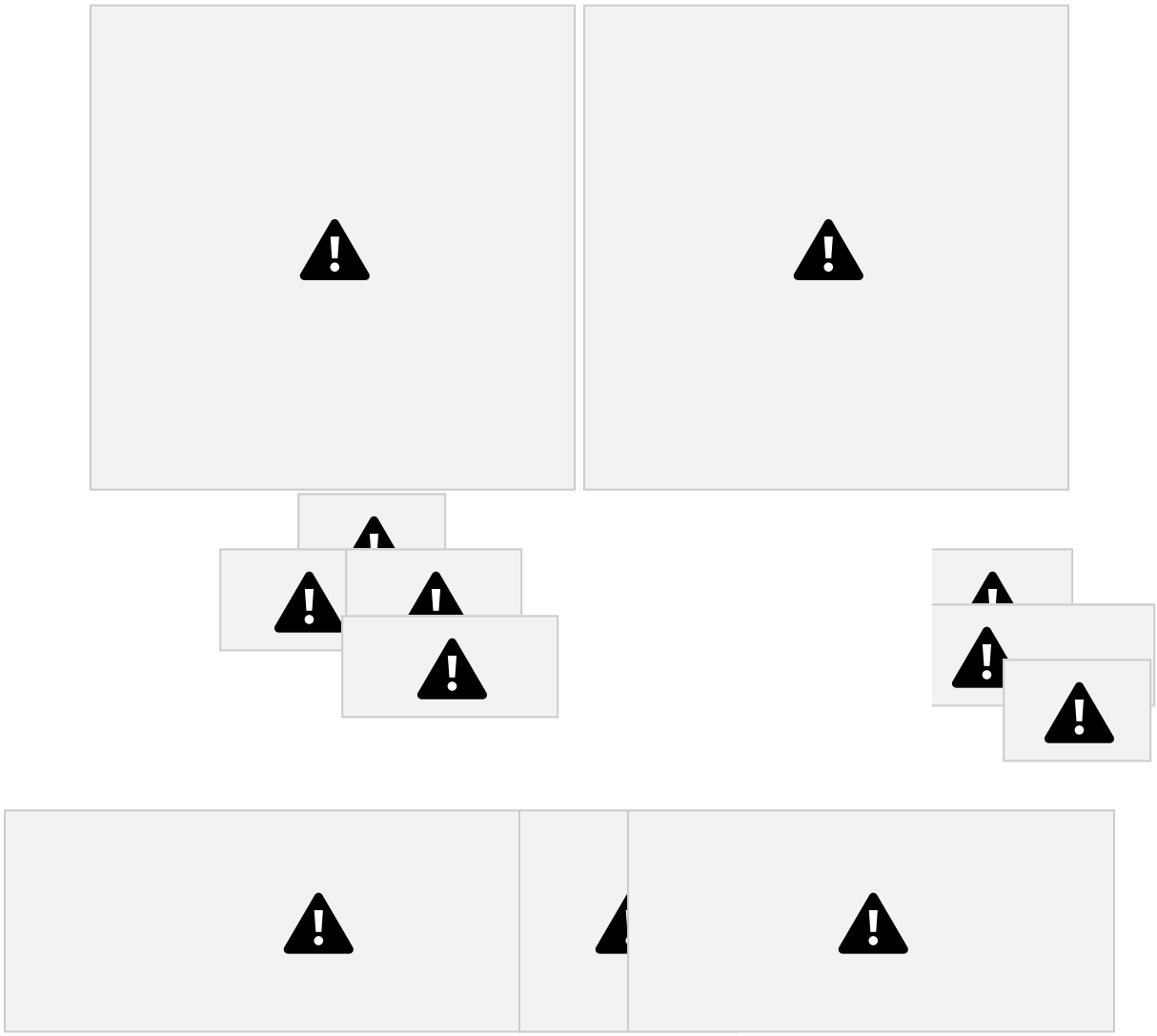
Villefranche

vs

BRIGHTON (JHS)

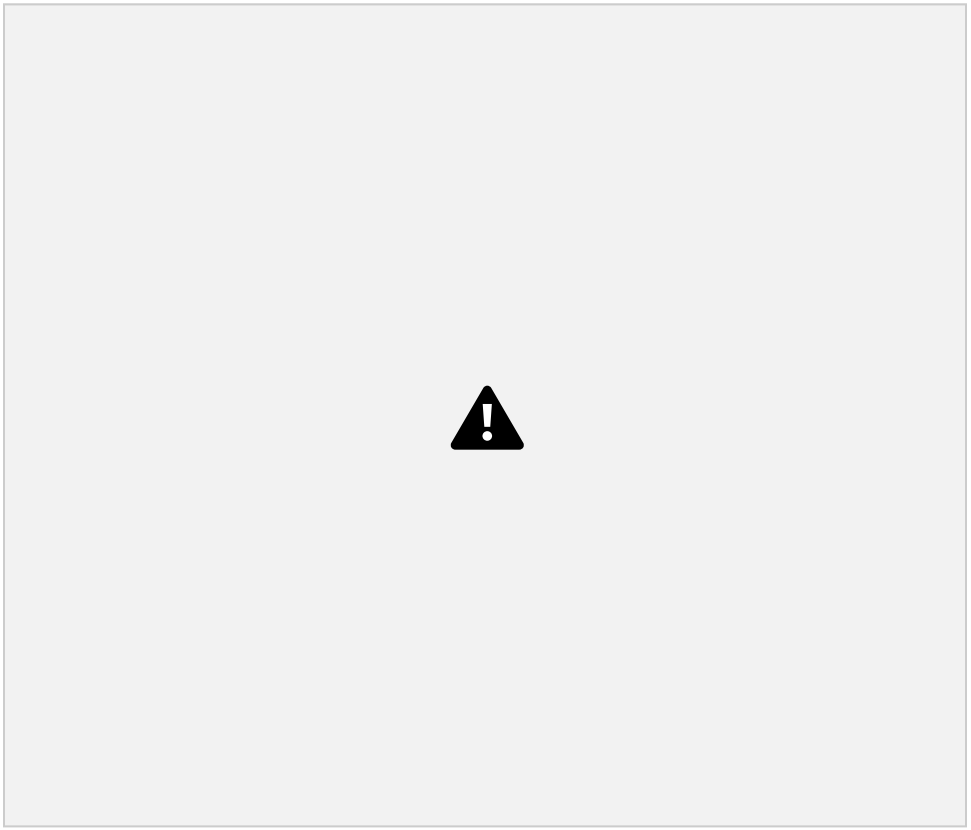


VILLEFRANCHE (EDS-HT)



Villefranche *vs* Brighton

Villefranche vs Brighton



- ✔ A link between JHS and EDS HT seems to exist in familial cases
- ✔ Villefranche criteria are more common in children
- ✔ Brighton criteria are more common in symptomatic adults and elder
- ✔ **Villefranche and Brighton criteria may be complementary in the**

extended family

(Castori et al., Am J Med Genet A 2014)

⚠

Reasons supporting a "spectrum"

… Ranging from gJHM, to JHS, EDS-HT, JHS/EDS-HT, JHS/EDS-HT + disability, etc

1. Beighton score reduces by age
2. Pain and joint instability complications may be absent and age dependent
3. Cutaneous manifestations may modify by age
4. Acquired (traumas, sport activities, etc) and constitutional (e.g. sex hormones) factors may affect the symptomatic trajectories of gJHM

Reasons supporting a "syndrome"

… Separating patients with a convincing pleiotropic syndrome predisposing to multiple symptoms/disability from individuals with a/oligosymptomatic gJHM

1. Having more homogeneity for management issues
2. Having more homogeneity for therapeutic issues
3. Having more homogeneity for research issues
4. Maintaining a coherence within the EDS nosology
5. Attracting more attention from the scientific community 6. Optimizing economic, professional and research resources

The spectrum and the syndrome

COMPLICATIONS

Psychological distress

GI functional disorders

Cardiovasculal dysautonomia

Sporadic/non Physical disabilities

Asymptomatic **gJHM** *(asset?)*

Pelvic/bladder dysfunctions

Complex **EDS-HT**

c **gJHM**

Oligosymptomati *Mendelian* **JHS** *Familial* **JHS/EDS-HT**

Asymptomatic

EDS-HT

PHENOTYPES

The two "lacking" agreements

… While the term hEDS will probably substitute EDS-HT and, perhaps, JHS….

Where can we put the *vertical* cut-off separating **hEDS** from **non-syndromic gJHM**?

Where can we put the *horizontal* cut-off separating "**mild**" **hEDS** from "**complex**" **hEDS**?

In the meanwhile…. The

Italian

way **A convincing diagnosis of hEDS may be fixed in presence of:**

Both major Villefranche criteria + one or more minor Villefranche criteria ***Or***

Both major Brighton criteria + overt cutaneous involvement ***Or***

Both major Brighton criteria + one or more first-degree relatives with an independent diagnosis of hEDS

Or

One major Brighton criterion + two or more minor Brighton criteria + an overt cutaneous involvement OR one or more first-degree relatives with hEDS ***Plus***

Clinical-molecular exclusion of partially overlapping conditions (e.g. cEDS, vEDS, LDSs, mild OI)

In the meanwhile…. The

Italian

way **Incomplete diagnoses include:**

Both major Villefranche criteria only (asymptomatic) = ***possible hEDS***

diagnostic follow-up for symptomatic screening (mostly limb pain and dislocations; possible transition to hEDS)

Both major Brighton criteria only = ***not otherwise defined JHS***

Referral to the musculoskeletal specialist and request for first-degree relatives' assessment (possible transition to hEDS)

1 major and 2 or more minor Brighton criteria only = ***not otherwise defined JHS***

Referral to the musculoskeletal specialist and request for first-degree relatives' assessment (possible transition to hEDS)

4 or more minor Brighton criteria only = ***not otherwise defined JHS*** Referral to the musculoskeletal specialist

gJHM and other combinations of symptoms = ***oligosymptomatic gJHM*** Referral to the pertinent specialist(s)

In the (near) future….?

hEDS

New Criteria - stricterthan the Villefranche and Brighton criteria applied isolately

"Complex" hEDS

hEDS new criteria *plus* one or more chronic disabling features (?)

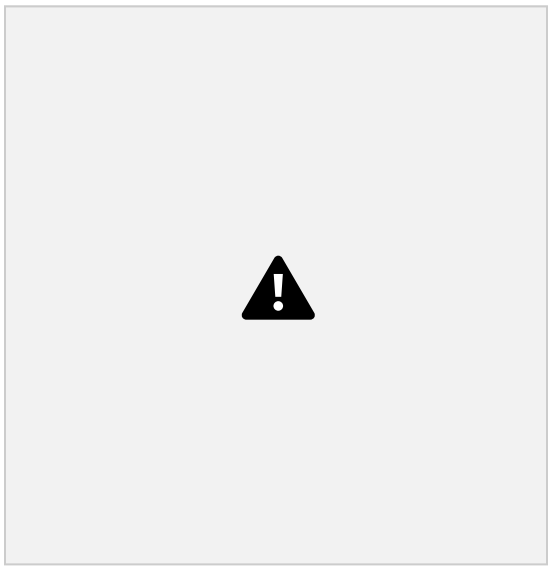
Generalized joint hypermobility disorders

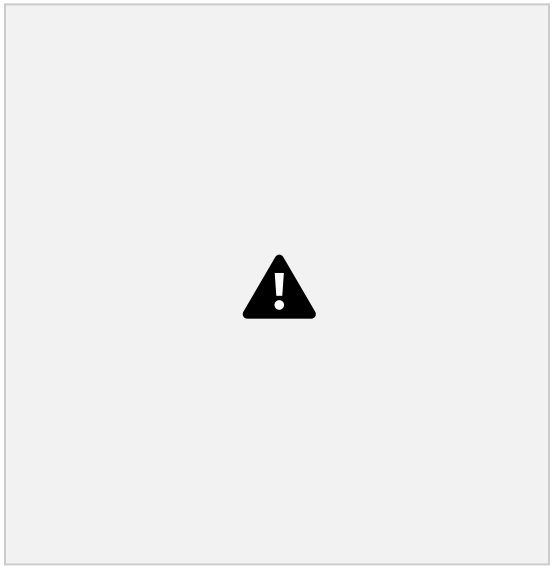
A term for incomplete phenotypes comprising:

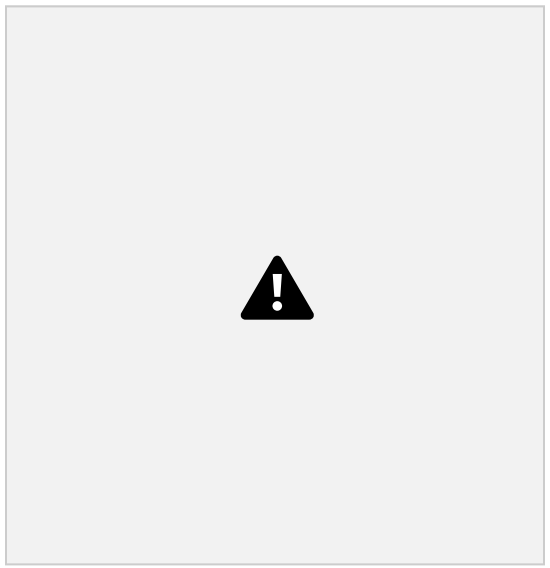
1. *Possible hEDS* (e.g. children with gJHM, other structural changes but too few symptoms)
2. *Not otherwise defined JHS* (e.g. symptomatic patients with gJHM and isolated musculoskeletal system)
3. *Oligosymptomatic gJHM* (i.e. patients with gJHM and single or a few statistically associated symptoms – mostly extra

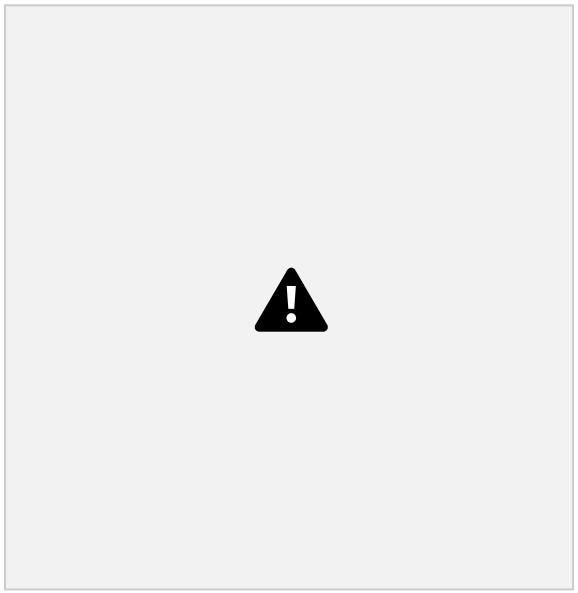
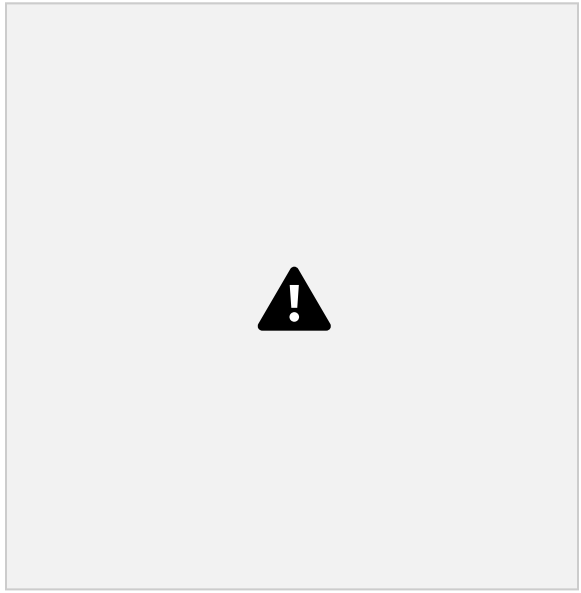
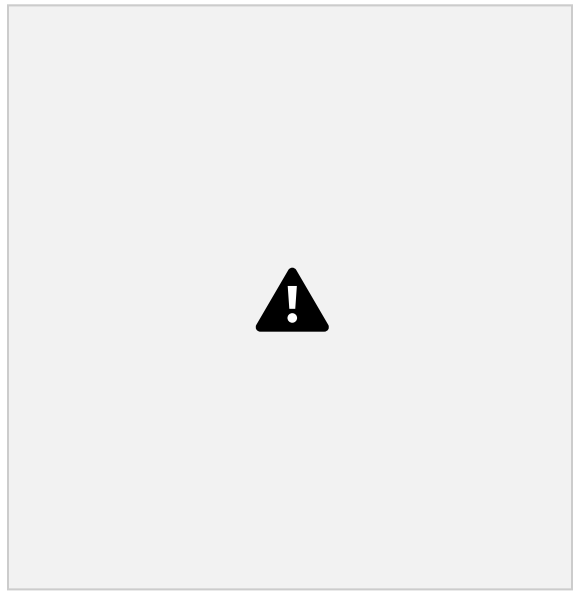
musculoskeletal)

The hope of the molecular research







The putative molecular basis of hEDS:

Aspecific phenotype caused by private/rare mutations in known genes?

A discrete phenotype caused by mutations in still unknown genes? A mixture of various phenotypes linked to mutations in different genes?

In the (far) future….?

Molecular subclassification of hEDS (i.e. molecular tests) Expansion of the molecular nosology of EDSs

Accurate family counselling and presymptomatic testing Molecularly-driven prognostication

System-based assessment by laboratory tools (i.e. clinical tests) More objective severity scoring

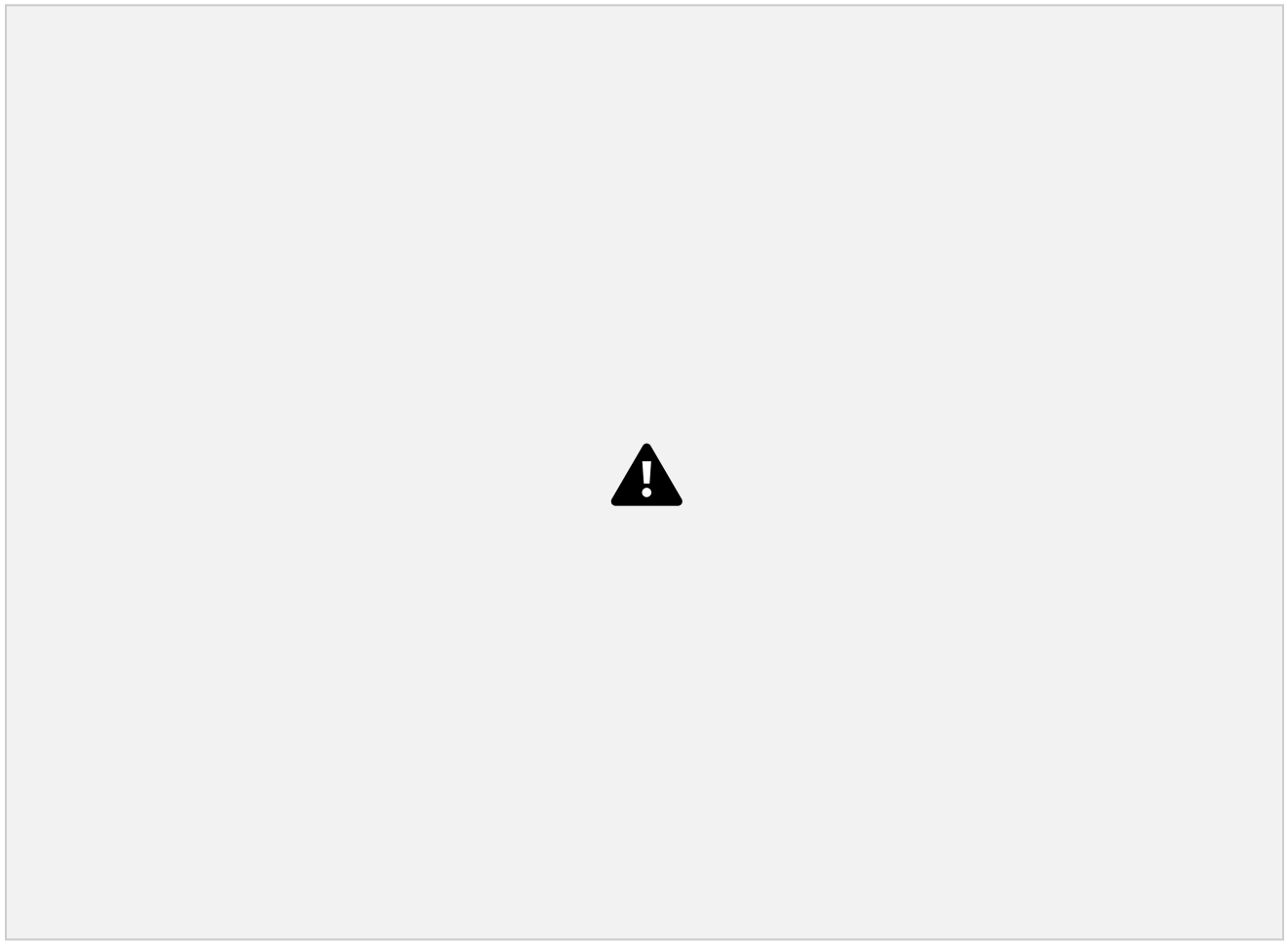
More objective prioritization of cure

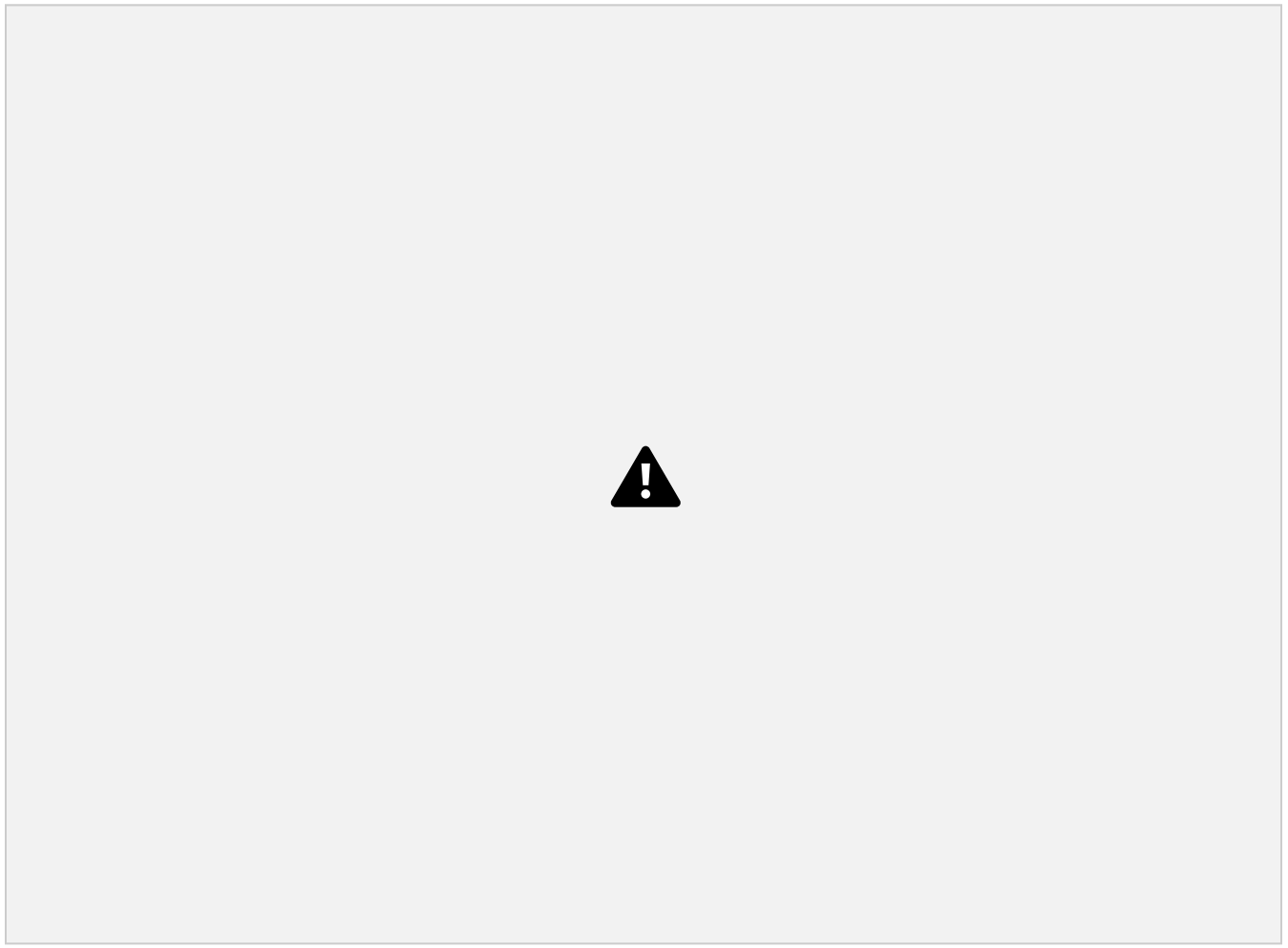
More rigorous clinical trials

Secondary manifestations of generalized joint hypermobility

Secondary and primary

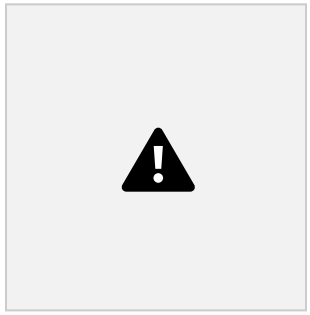
manifestations





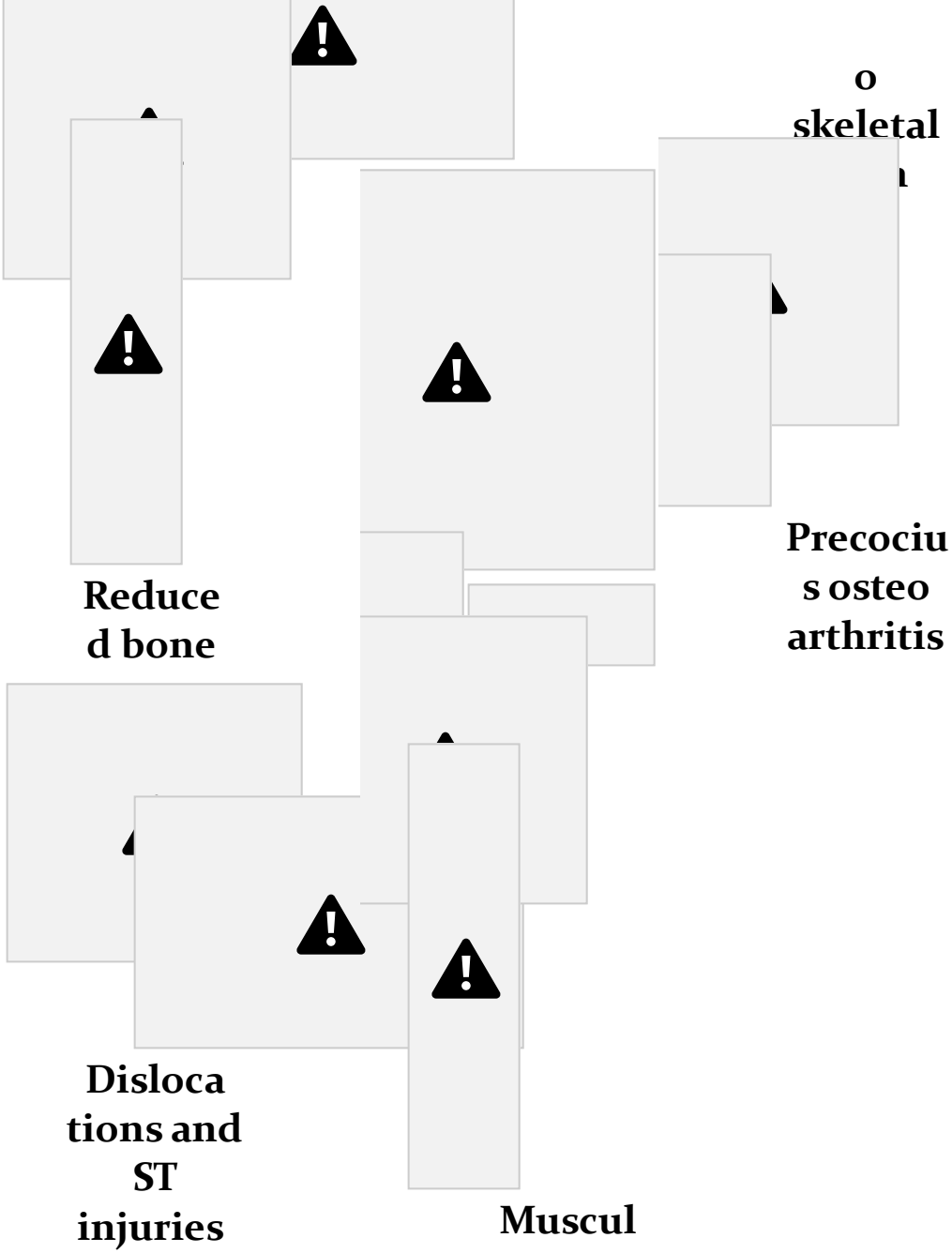
(Castori & Colombi, 2016)

***Phenotypic continuity** of systemic hereditary connective tissue disorders*



Secondary manifestations of gJHM

Articular dysfunctions

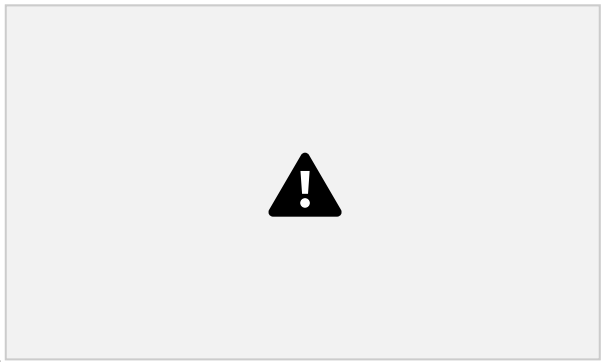

o
skeletal
Precociu
s osteo
arthritis
Reduce
d bone
Disloca
tions and
ST
injuries
Muscul

Deform
a tions

Secondary manifestations: Pain

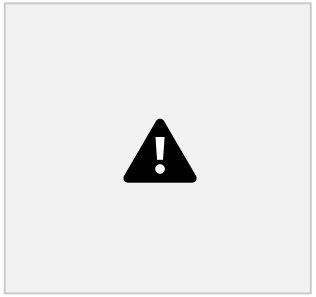
gJHM

*
**



Microtraumatism

Macrotraumatism



Premature osteoarthritis

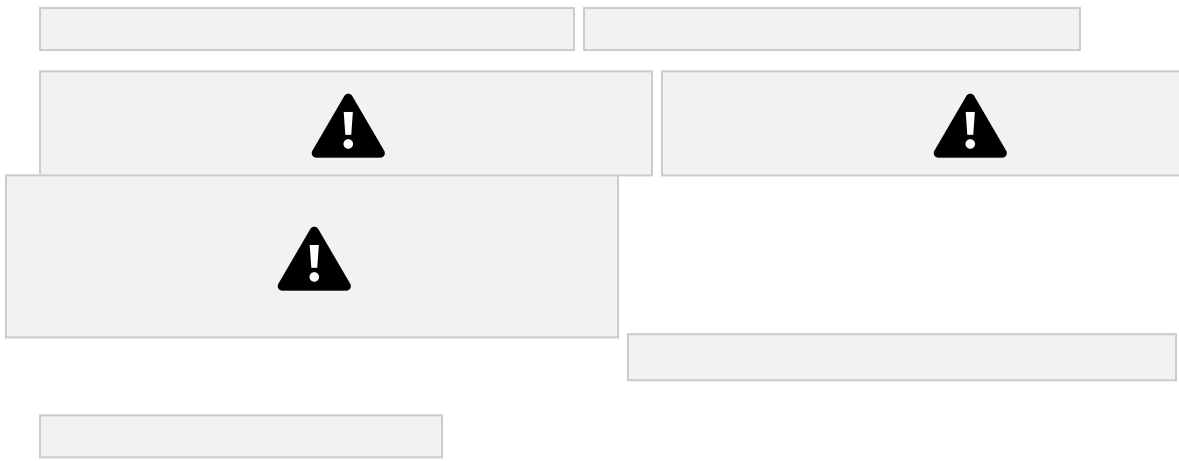
Loco-regional dysfunctions

Dislocations

Soft-tissue injuries

Secondary manifestations: Pain

gJHM



Peripheral pain

sensitivity

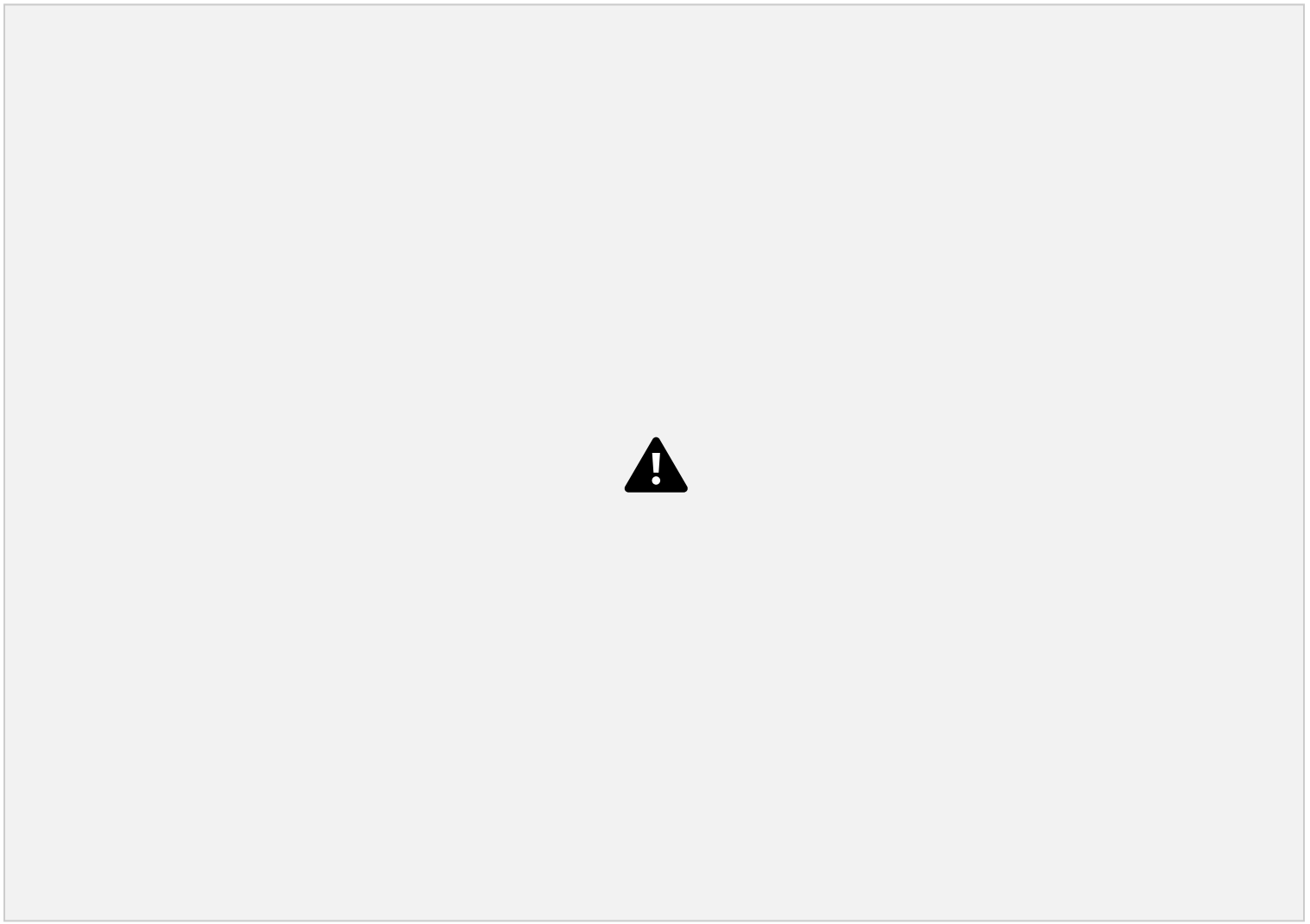
Central

Maladaptive cognitions

pain
sensitivity

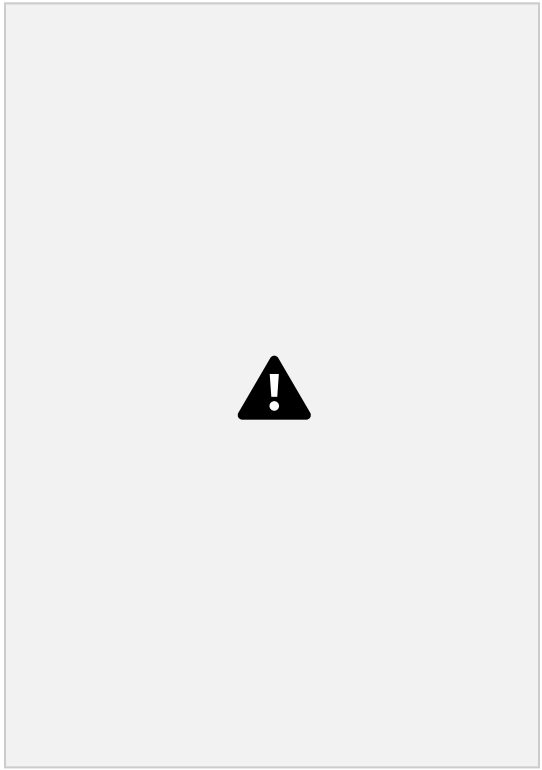
(Castori et al., 2013; Rombaut et al., 2014; Di Stefano et al., in press)

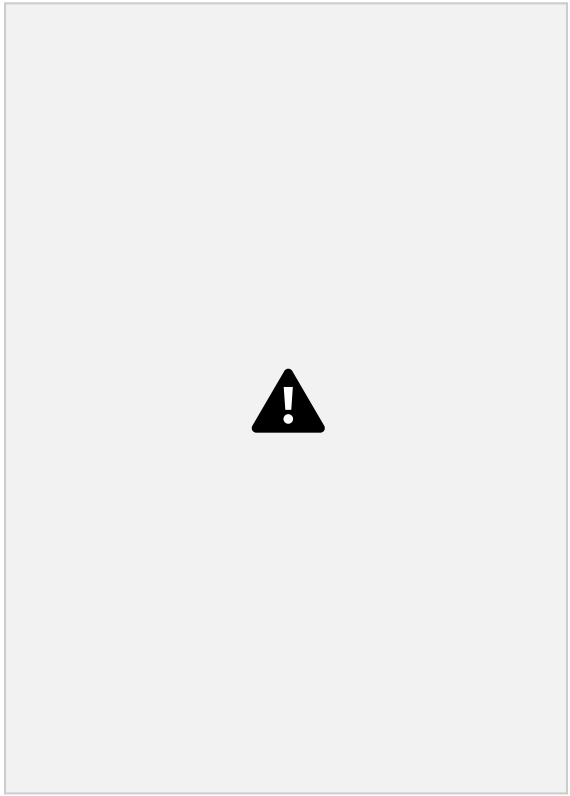
Secondary manifestations: Pain



(Castori, EOOD, in press)

Secondary manifestations: Pain

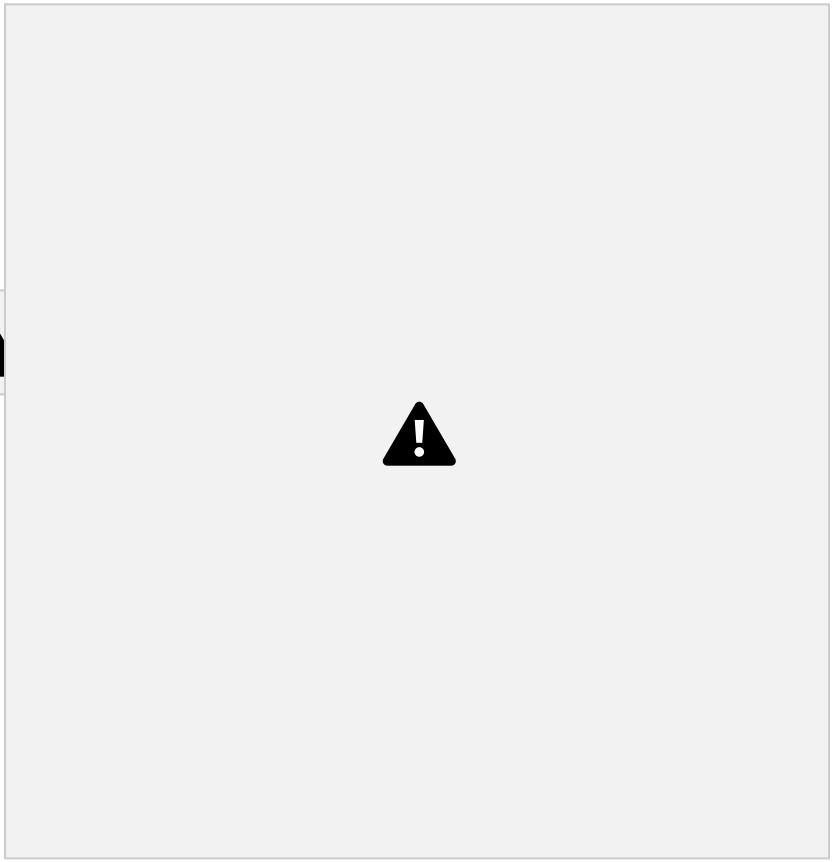


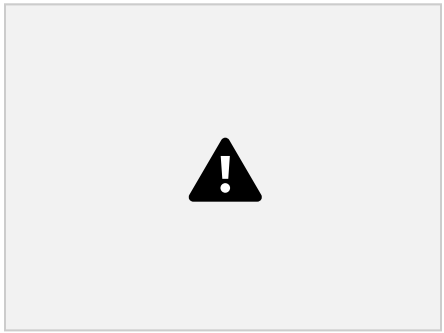


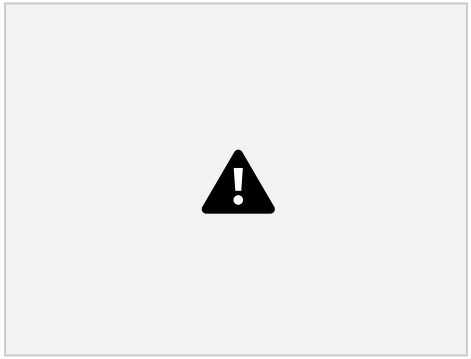
Secondary manifestations: Pain

Widespread pain	Feature	Prerequisite
Nature of the diagnosis	Longitudinal	Punctual
Diagnostic criteria	Signs, symptoms and family history	Symptoms
Setting	Highly specialistic	Non specialistic
Pathogenesis	Systemic	Neurologic
Transmission	Mendelian	Multifactorial, polygenic
Prognostic factors	Multifactorial	Psychologic, psychiatric
Prevention	Possible	Not possible
Treatment	Multidimensional	Multidimensional

Secondary manifestations: Pain





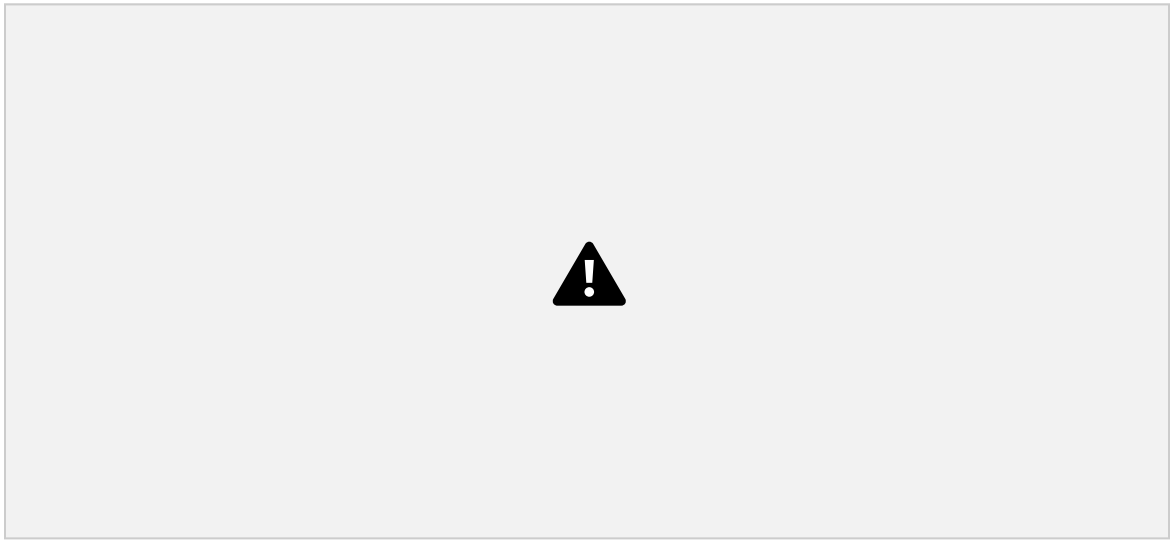


Examples of painkillers in adults with EDS

Ibuprofen	1,200 mg	1,800 mg
Naproxen	1,000 mg	1,000 mg
Paracetamol	1,200 mg	3,000 mg
Amitryptilin	10-50 mg	300 mg
Gabapentin	150-900 mg	300-3,600 mg
Diazepam	10-30 mg	40 mg
Tramadol	25 mg x 4-6 times	300 mg
Codein + paracetamol	30 mg + 500 mg	X 4-6 times

Secondary manifestations: Pain *(Castori,*

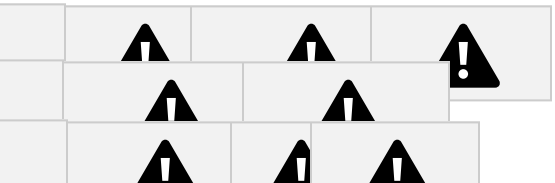
EOOD, in press)



Secondary manifestations: deformations

Increased molding of the musculoskeletal system under:

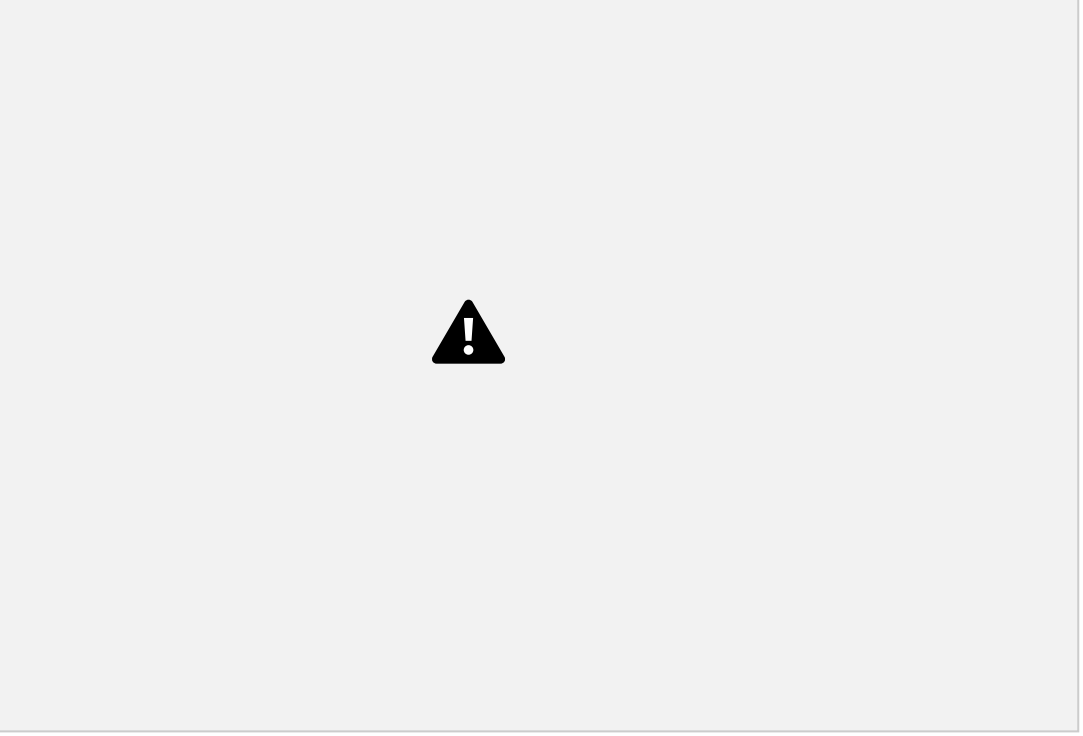
1. Intrauterine mechanical forces
2. Gravity and body weight
3. Repetitive traumas



4. Activities and sports

5.  Handedness

Secondary manifestations: bone mass



Reduced bone mass

✔*Amplification of musculoskeletal complaints*

✔*Increased fracture risk?*

Neuro-psychiatric/developmental attributes of generalized joint

hypermobility

Neurodevel./psychologic

features

Generalized joint hypermobility

Neuro

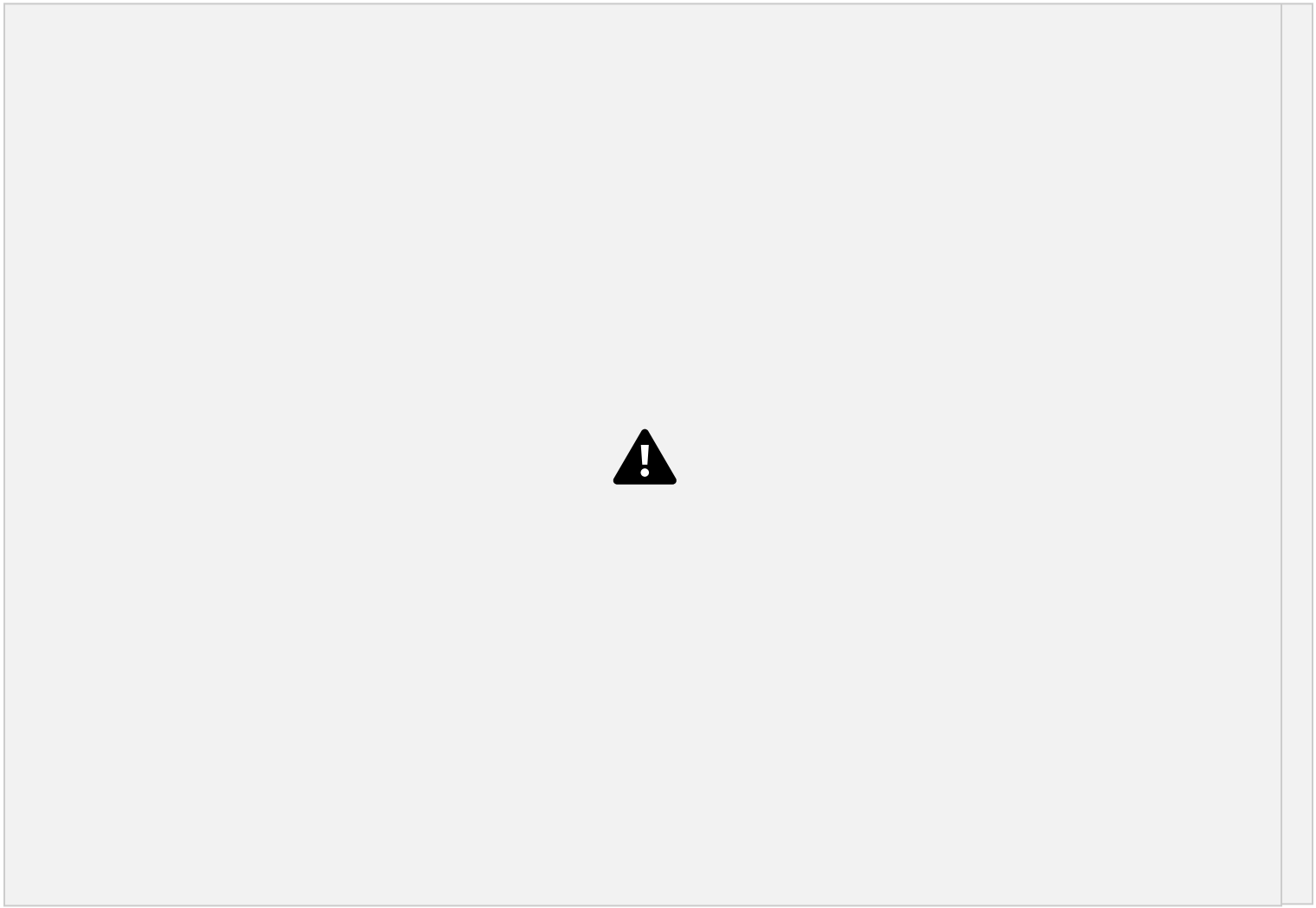
s

Ehlers-Danlo

syndrome(s)

developmental and neuro

psychologic attributes



reports

Anxiety disorders
✔ In EDS in general
✔ Up to 72% in adults with JHS/EDS-HT (less common in classic EDS)
✔ Lumley et al., 1994; Murray et al., 2013; Hershenfeld et al., 2015
Depression
✔ In EDS in general
✔ up to 70% in adults with JHS/EDS-HT (less common in classic EDS)
✔ Lumley et al., 1994; Murray et al., 2013; Hershenfeld et al., 2015
Obsessive-compulsive personality disorder
✔ Up to 10.6% in adults with JHS/EDS-HT
✔ Pasquini et al., 2014
Autistic spectrum disorders
✔ Fehlow and Tennstedt, 1985; Tantam et al., 1990; Sieg, 1990; Takei et al., 2011
Schizofrenia
✔ Sienaert et al., 2003
Possibility for an incorrect diagnosis of *conversion disorder*
✔ Barnum, 2014
Eating and weight problems

✔ Baeza-Velasco et al., 2015

Neuropsychiatric features are more common in presence of chronic neurological symptoms/disabilities

Case-control studies

(Sinibaldi et al., 2015)

Body-brain connections

Congenital laxity of tissues

Sensory dysfunction

brain volumetric changes

Specific

(Eccles et al., 2012)

(Bulbena et al.,

Pain & Fatigue (Hershenfeld et al., 2015)

2015)

Dysautonomia (Eccles et al., 2015)

Psycho

c manifesta

Pleiotropy (Sinibaldi et al., 2015)

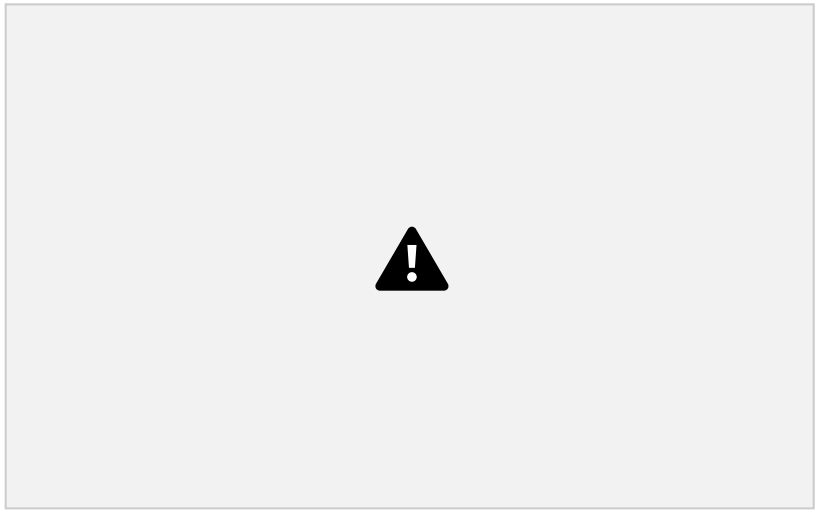
pathologi

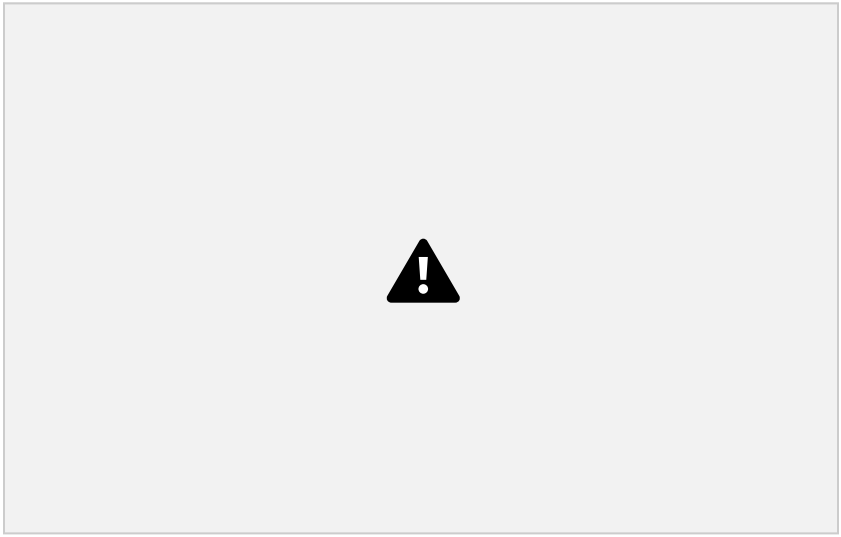
Body-brain connections

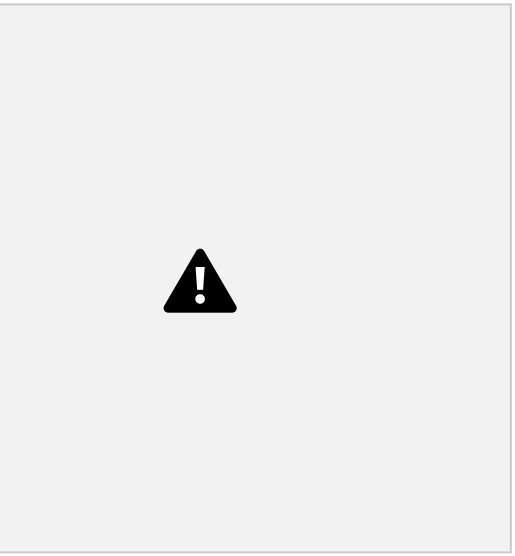
“Bilateral amygdala volume was significantly greater in the hypermobile group than in the non hypermobile group”.

“The hypermobile group as a whole also display decreased anterior cingulate and left parietal cortical volume while the degree of hypermobility correlates negatively with both superior temporal and inferior parietal volume”.

Developmental coordination disorders







gJHM in DCD

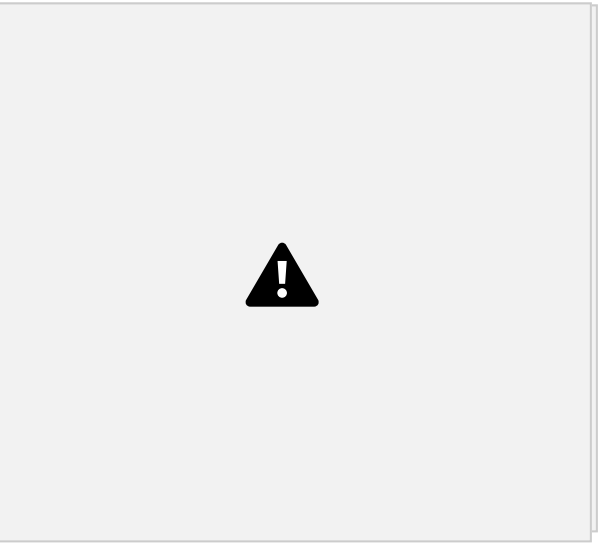
(Benady&Ivanans, 1978, Jaffe et al., 1988, Jelsma et al., 2013; Celletti et al., 2015)

1. gJHM is more common in children with motor delay/DCD
2. Persistence of gJHM affects motor outcome

JHS/EDS-HT in DCD

(Kirby et al., 2005; Kirby&Davies, 2007)

1. JHS/EDS-HT symptoms are reported in 37% DCD children (>5 times vs GP)



gJHM

(Adib et al., 2005; Easton et al., 2014; Castori et al., 2014)

1. Poor coordination, clumsiness, simple motor delay and DCD are common in these conditions

DCD in JHS/EDS-HT or

Early studies: gJHM & motor delay

Benady and Ivanans (1978)

Population: 9 children with motor delay

Study design: cross-sectional

Conclusions: gJHM characterized a “benign” form of simple motor delay associated with dislocation of the hip and positive family is of gJHM and motor delay

Jaffé et al.(1988)

Population: 717 “healthy” children

Study design: longitudinal

Conclusions: simple motor is more common in presence of gJHM and reduction of joint mobility improves motor competence in a 6-month period.

Tirosh et al.(1991)

Population: 717 “healthy” children

Study design: case-control, longitudinal

Conclusions: among toddlers ascertained for motor delay, those showing gJHM had a less favorable motor outcome.

gJHM in DCD

Celletti et al.(2015)

Population: 41 children with DCD

Study design: cross-sectional

Conclusions: gJHM is present in ~50% children. gJHM associates with frequent falls, easy bruising , motor impersistence, sore hands for writing, ADHD, constipation, arthralgias/myalgias, narrative difficulties, and atypical swallowing.

Morrison et al. [2013]

Population: 14 children with DCD

Study design: cross-sectional

Conclusions: DCD chidren commonly present lower limb hypermobility and pes planus and these features may be major contributors to abnormal gait typical.

JHS/EDS-HT features in

DCD

Kirby et al. (2005)

Population: 58 children with DCD, 68 children with JHS

Study design: cross-sectional, case-control

Conclusions: motor competence is nearly overlapping between children with DCD and those with JHS.

Kirby and Davis (2007)

Population: 27 children with DCD and 27 normally developing children Study design: cross-sectional, case-control

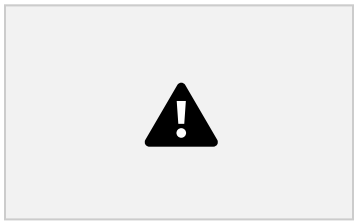
Conclusions: JHS/EDS-HT features have a 5-fold rate in children with DCD compared to normally developing children.

Jelsma et al. (2013)

Population: 36 children with DCD and 352 normally developing children Study design: cross-sectional, case-control

Conclusions: Beighton score is higher among chidren with DCD compared to the others.

Coordination and motor features in gJHM



Easton et al.(2014)

Population: 119 children with gJHM

Study design: cross-sectional

Conclusions: Motor competence was low in 32.8% of patients and very low in 18.4%. Motor difficulties were more common in males and in younger subjects.

Schubert-Hjalmarsson et al. (2012) and Falkerslev et al. (2013) Population: children with gJHM vs children without gJHM

Study design: case-control

Conclusions: children with gJHM have reduced balance compared to healthy controls.

Castori et al. (2014) and (Hershenfeld et al., 2015)

Population: 23 children with JHS/EDS-HT and 106 adults with EDS

Study design: cross-sectional

Conclusions:: ADHD has a high rate in EDS.

Coordination and motor features in EDS

Hunter et al.(1998)

Population: 414 patients with EDS

Study design: cross-sectional, questionnaire

Conclusions: hearing, voice, speech and swallowing difficulties are common in EDS.

Adib et al.(2005)

Population: 125 children with JHS

Study design: cross-sectional

Conclusions: clumsiness (48%), poor coordination (36%), learning

difficulties (14%), dyspraxia (7%), dyslexia (2%), weakness (39%) and muscle wasting (26%).

Castori et al.(2014)

Population: 20 children with JHS/EDS-HT from familial cases

Study design: cross-sectional

Conclusions: 50% children have DCD.

Interpretations

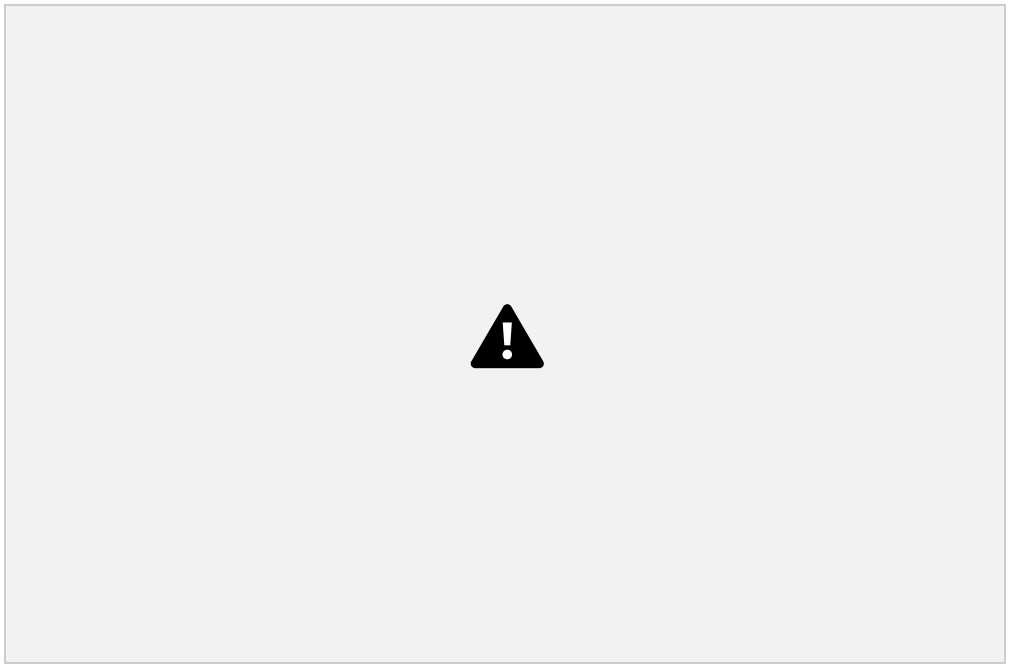
✔ gJHM may be a predisposing factor for DCD and other coordination and simple motor features in the general population

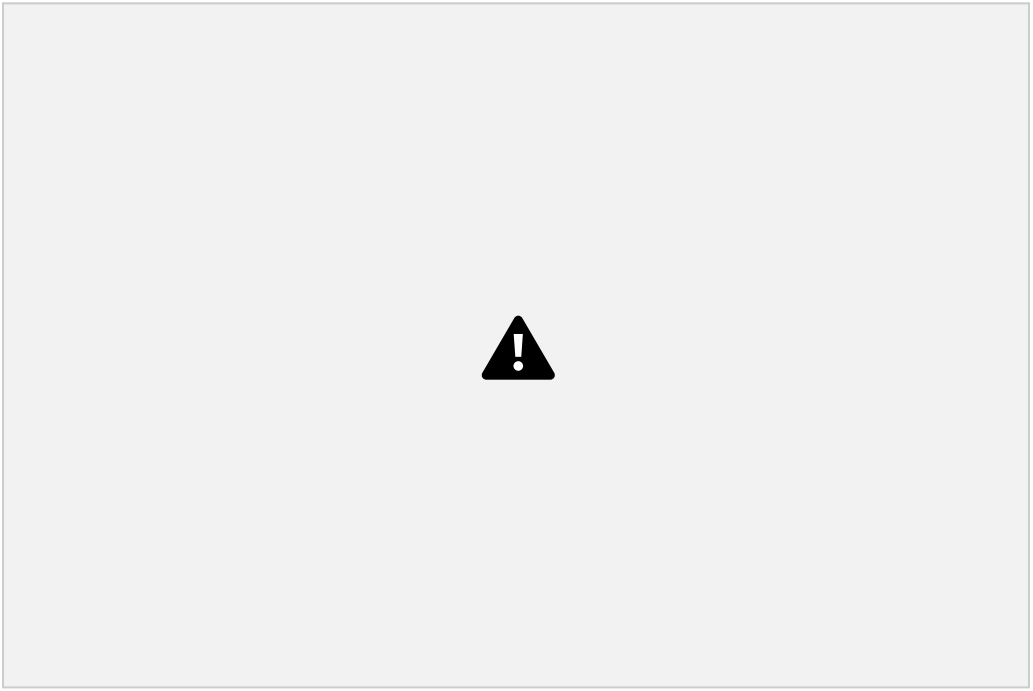
✔ EDS

patients, especially those with JHS/EDS-HT, frequently manifest DCD.

✔ In selected cases, congenital laxity of tissues may be a specific etiopathogenetic basis of DCD.

Proprioceptive impairment





Proprioception is often impaired:

- At knees in children and adults (Hall et al., 1995; Sahin et al., 2008; Fatoye et al., 2009; Rombaut et al., 2010; Pacey et al., 2014)
- At proximal interphalangeal joints of the fingers in adults (Mallik et al., 1994)

Proprioceptive sensitivy at the non-dominant hand is lower in EDS patients compared to controls (Clayton et al., 2013; 2015)

Attention deficit/hyperactivity disorder

Harris (1998)

Population: 200 children with ADHD

Study design: editorial

Conclusions: Generalized joint hypermobility is extremely common among children with ADHD

Koldas-Dogan et al. (2011) and Shiari et al. (2013)

Population: 54 and 86 children with ADHD vs 36 and 86 healthy

children Study design: case-control

Conclusions: Generalized joint hypermobility is more common in children with ADHA (31.5% and 74.4%) compared to controls (13.9% and 12.8%)

Cederlöf et al. (2016)

Population: 1171 EDS patients (Nationwide registry study)

Study design: case-control, registry

Conclusions: ADHD is a co-morbility in 4.3% of EDS cases (RR: 5.6); ADHD is more common also in the relatives of EDS patients

DCD, AD(H)D,

gJHM and EDS

General population

gJHM (+/- HCTD)

Co-morbidity AMPLIFIED

Co-morbidity

Pathogenesis

Generalized joint hypermobility

(Iatridou et al., 2014)

Vestibular

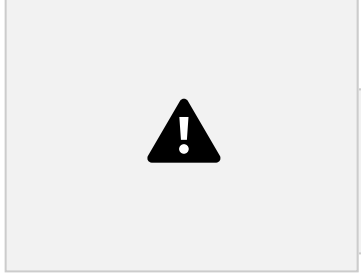
dysfuction

Lack of

Co-morbidity with AD(H)D

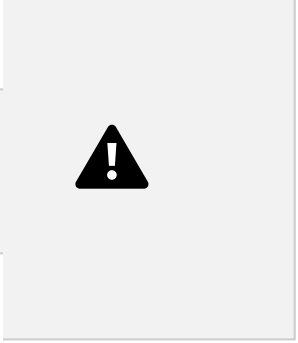
(Sinibaldi et al., in preparation)

Reduced muscle



proprioception

(e.g. Clayton et al., 2015)

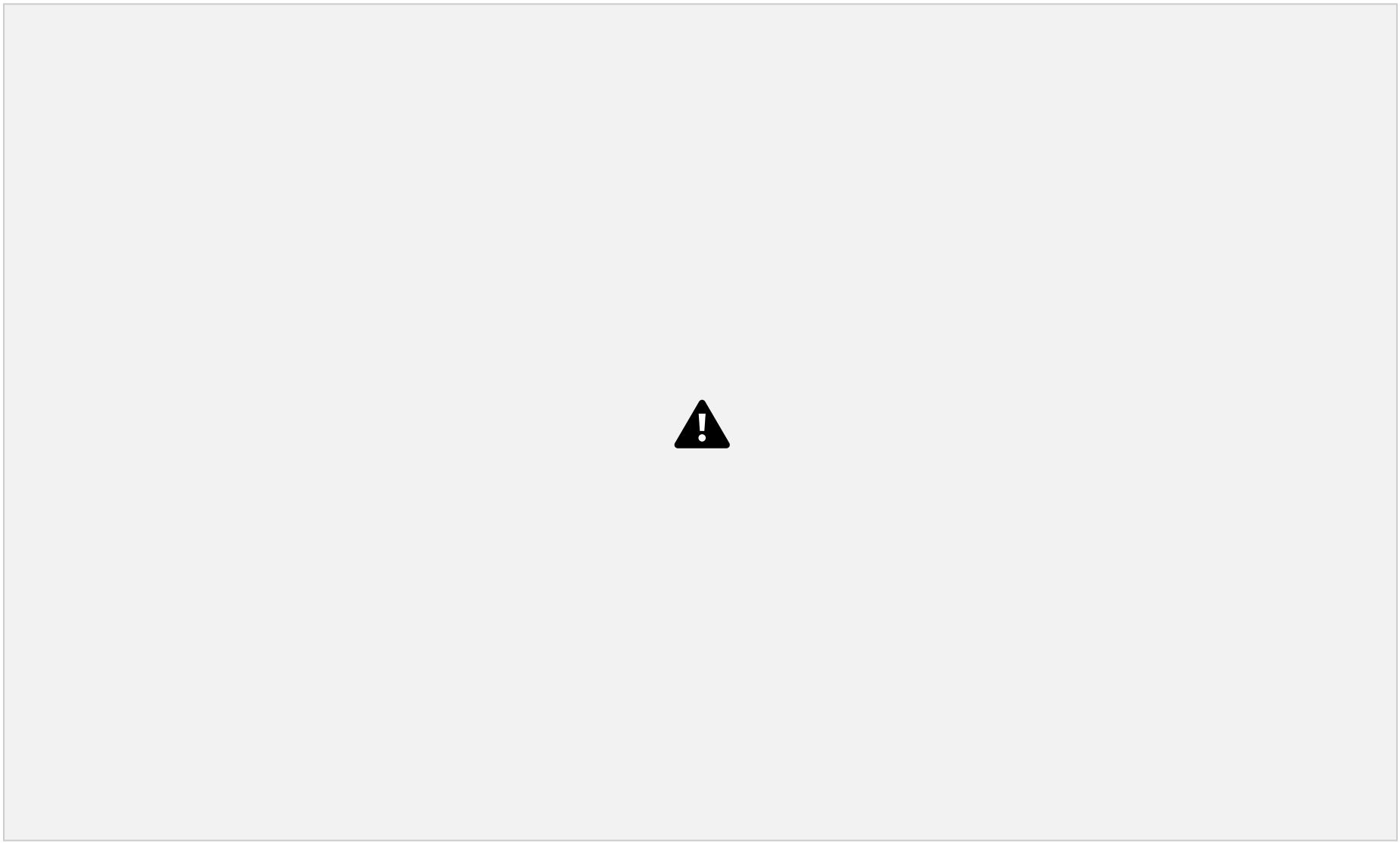


Coordination difficulties

tone

(Castori et al., 2013)

Recommendations for children with EDS + DCD



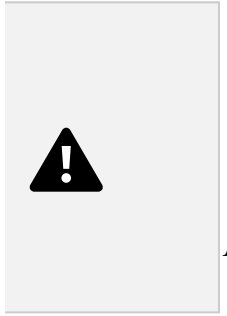
Connections of the

“neuroconnective phenotype”

Persona
lity
disorders


JHS
and
DCD
Depres
gJHM
AD(H)D
Eating

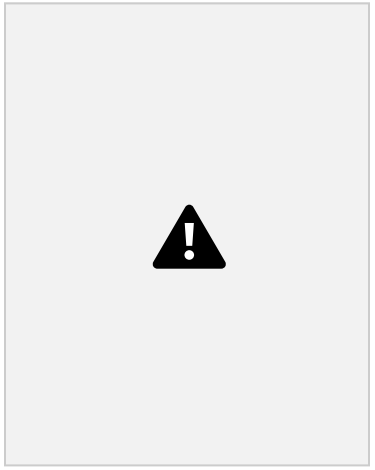
and
weight
disorders



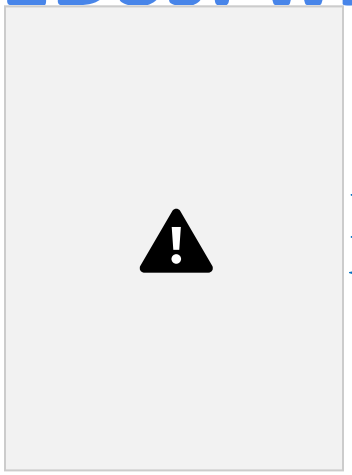
ance
coping
strategies

Avoid

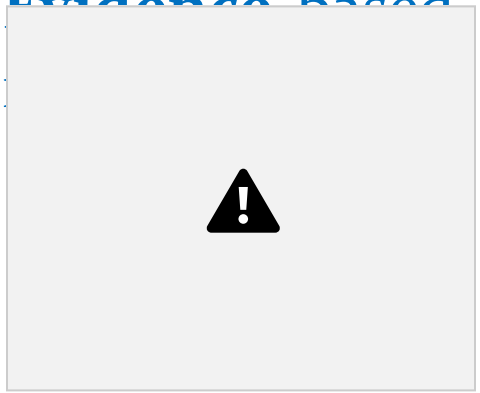
Conclusions



EDSs: why to differentiate?



Experience
based medicine



Precision
medicine

Exclusion or integration?

Utility of the "correct" diagnosis ✔

To **prioritize** assistance among "modules"

✔ To **personalize** assistance within the same "module"

✔ To address **pregnancy and family** issues

Not all sHCTDs have the same expression in any given organ/apparatus

Not all patients with the same sHCTD have the same degree of organ-specific involvement

Not all sHCTDs have the same genetic transmission, pregnancy-related complications and intrafamilial variability

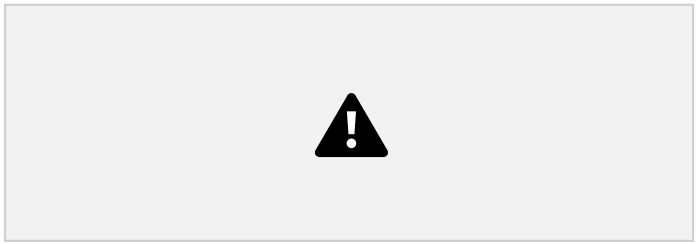
Modules of assistance

Musculoskeletal and Pain issues

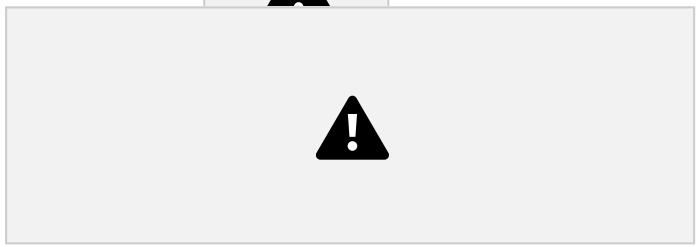
Neurodevelopmental issues

Cardiovascular and

autonomic issues



Urogynecological



Cognitive/psychiatric

issues

Gastrointestinal

issues

Mucocutaneous and fascia issues

 Family and pregnancy issues  

What can we do for EDS patients?

Primary prevention *"to prevent disease or injury before it ever occurs"*	- (+/-)
Secondary prevention *"to reduce the impact of a disease or injury that has already occurred"*	++
Tertiary prevention *"to soften the impact of an ongoing illness or injury that has lasting effects"*	+
Treatment	+/-

What can we do for EDS patients?

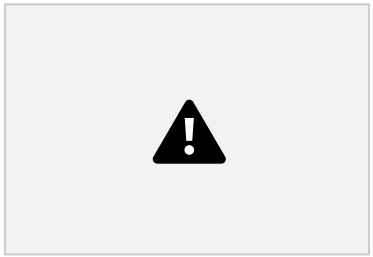
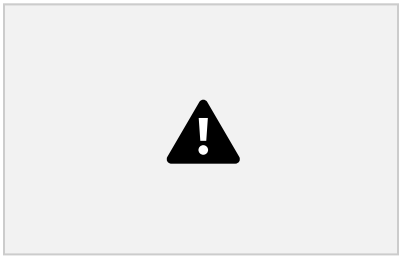
- ✔ **COORDINATION OF CARE** (multidisciplinarity)
- ✔ **INTERDISCIPLINARITY** (multispecialistic teams by topic)
- ✔ **RISING AWARENESS** (dissemination of knowledge)
- ✔ **RESEARCH** (clinical, basic, translational)

THANKS!

Acknowledgments



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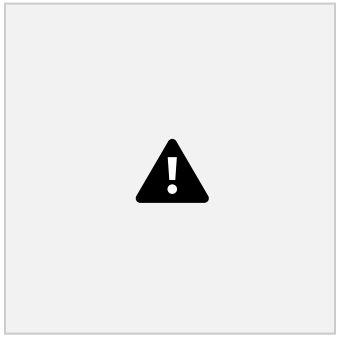
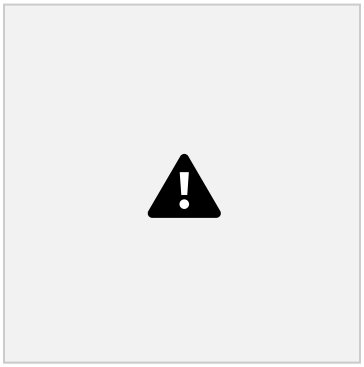
Dr. C. Blundo
Dr. A. Petrucci
Dr. M. Calvani
Dr. F. Pierucci
..and others...

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