# Supplementary Materials

## Supplementary Table 1. Assessment of generalized joint hypermobility and joint hypermobility syndrome (JHS) (adapted from references [1-6]).

|  |
| --- |
| **Five‐point questionnaire for generalized joint hypermobility (screening tool)** |
| Answering yes to two or more of these questions suggests hypermobility with sensitivity of 85% and specificity of 90% |
| 1. Can you now (or could you ever) place your hands flat on the floor without bending your knees? 2. Can you now (or could you ever) bend your thumb to touch your forearm? 3. As a child, did you amuse your friends by contorting your body into strange shapes or could you do the splits? 4. As a child or teenager, did your kneecap or shoulder dislocate on more than one occasion? 5. Do you consider yourself “double‐jointed”? |
| **Beighton score (clinical assessment of joint hypermobility). Score 0‐9.** |
| 1. Passive dorsiflexion of the little fingers beyond 90 degrees (one point for each hand). Two points 2. Passive apposition of the thumbs to the flexor aspects of the forearms (one point for each thumb). Two points 3. Hyperextension of the elbows beyond 10 degrees (one point for each elbow). Two points. 4. Hyperextension of the knees beyond 10 degrees (one point for each knee). Two points. 5. Forward flexion of the trunk with knees fully extended so that the palms of the hands rest flat on the floor. One point. |
| **1998 Brighton Classification for JHS. Diagnostic criteria for joint hypermobility syndrome.** |
| Major criteria |
| 1. Beighton score of 4/9 or greater (either currently or historically) 2. Arthralgia for longer than three months in four or more joints |
| Minor criteria |
| 1. Beighton score of 1, 2, or 3/9 (0, 1, 2, or 3 if aged 50 and above) 2. Arthralgia (for three months or longer) in 1‐3 joints, back pain (for three months or longer), or spondylosis, spondylolysis, spondylolisthesis 3. Dislocation/subluxation in more than one joint or in one joint on more than one occasion 4. Soft tissue rheumatism: three or more lesions (e.g., epicondylitis, tenosynovitis, bursitis) 5. Marfanoid habitus (tall, slim, span/height ratio >1.03 upper:lower segment ratio <0.89, arachnodactyly [positive Steinberg/wrist signs]) 6. Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring 7. Eye signs: drooping eyelids, myopia, or antimongoloid slant 8. Varicose veins, hernia, or uterine/rectal prolapse |

## Supplementary Table 2. Mixed model results for gender with each symptom.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Pain** | | **Bloating** | | **Diarrhea** | | **Constipation** | | **Average score** | |
|  | ***beta*** | ***p*** | ***beta*** | ***p*** | ***beta*** | ***p*** | ***beta*** | ***p*** | ***beta*** | ***p*** |
| *JHS # gender # time* |  |  |  |  |  |  |  |  |  |  |
| No # Female # Post low FODMAP diet | -0.83 | <0.0001 | -1.10 | <0.0001 | -0.88 | <0.0001 | -0.34 | 0.003 | -0.78 | <0.0001 |
| No # Male # Pre low FODMAP diet | 0.15 | 0.519 | -0.28 | 0.204 | 0.19 | 0.464 | -0.57 | 0.029 | -0.13 | 0.325 |
| No # Male # Post low FODMAP diet | -0.68 | 0.003 | -1.16 | <0.0001 | -0.65 | 0.014 | -0.48 | 0.067 | -0.74 | <0.0001 |
| Yes # Female # Pre low FODMAP diet | 0.56 | 0.014 | 0.27 | 0.231 | -0.33 | 0.212 | 0.38 | 0.148 | 0.22 | 0.092 |
| Yes # Female # Post low FODMAP diet | -0.57 | 0.013 | -0.93 | <0.0001 | -1.39 | <0.0001 | -0.003 | 0.992 | -0.72 | <0.0001 |
| Yes # Male # Pre low FODMAP diet | 0.50 | 0.666 | -1.23 | 0.274 | -1.78 | 0.179 | -0.13 | 0.923 | -0.66 | 0.315 |
| Yes # Male # Post low FODMAP diet | -0.75 | 0.511 | -1.23 | 0.274 | -1.78 | 0.179 | -1.13 | 0.394 | -1.22 | 0.063 |
| **Constant** | 3.25 | <0.0001 | 3.73 | <0.0001 | 1.78 | <0.0001 | 1.13 | <0.0001 | 2.47 | <0.0001 |
| **F test** | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 | |

FODMAP: Fermentable Oligosaccharide, Disaccharide, Monosaccharide and Polyol

## Supplementary Table 3. Mean differences post vs pre low FODMAP diet per variables JHS and gender.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Pain** | | **Bloating** | | **Diarrhea** | | **Constipation** | | **Average Score** | |
|  | ***contrast (95% CI)*** | ***SMD (95% CI)*** | ***contrast (95% CI)*** | ***SMD (95% CI)*** | ***contrast (95% CI)*** | ***SMD (95% CI)*** | ***contrast (95% CI)*** | ***SMD (95% CI)*** | ***contrast (95% CI)*** | ***SMD (95% CI)*** |
| *JHS # Gender* |  |  |  |  |  |  |  |  |  |  |
| No # Female | -0.83 (-1.06, -0.60)\*\*\* | -1.45 (-1.89, -0.99) | -1.10 (-1.33, -0.86) \*\*\* | -1.88 (-2.36, -1.40) | -0.88 (-1.13, -0.62) \*\*\* | -1.38 (-1.82, -0.94) | -0.34 (-0.57, -0.11)\*\* | -0.60 (-1.01, -0.19) | -0.78 (-0.92, -0.65) \*\*\* | -2.35 (-2.87, -1.83) |
| No # Male | -0.83 (-1.22, -0.44) \*\*\* | -1.43 (-2.19, -0.68) | -0.88 (-1.27, -0.49) \*\*\* | -1.51 (-2.28, -0.74) | -0.84 (-1.27, -0.41) \*\*\* | -1.32 (-2.07, -0.57) | 0.09 (-0.29, 0.47) | 0.16 (-0.51, 0.84) | -0.61 (-0..84, -0.39) \*\*\* | -1.84 (-2.64, -1.03) |
| Yes # Female | -1.13 (-1.52, -0.74) \*\*\* | -1.96 (-2.79, -1.13) | -1.20 (-1.59, -0.81) \*\*\* | -2.06 (-2.90, -1.22) | -1.05 (-1.49, -0.63) \*\*\* | -1.66 (-2.45, -0.87) | -0.38 (-0.76, -0.002)\* | -0.68 (-1.37, 0.02) | -0.94 (-1.17, -0.72) \*\*\* | -2.82 (-3.78, -1.86) |
| Yes # Male | -1.25 (-3.51, 1.01) | -2.16 (-4.69, 0.37) | 0.00 (-2.28, 2.28) | 0.00 (-3.92, 3.92) | 0.00 (-2.49, 2.49) | 0.00 (-3.92, 3.92) | -1.00 (-3.22, 1.22) | -1.76 (-4.83, 1.31) | -0.56 (-1.87, 0.75) | -1.68 (-4.83, 1.47) |

\*\*\* p < 0.001; \*\* p < 0.01; \* p < 0.05

## **References**

1. Beckers AB, Keszthelyi D, Fikree A, Vork L, Masclee A, Farmer AD, et al. Gastrointestinal disorders in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type: A review for the gastroenterologist. Neurogastroenterol Motil. 2017;29(8):e13013.

2. Botrus G, Baker O, Borrego E, Ngamdu KS, Teleb M, Gonzales Martinez JL, et al. Spectrum of Gastrointestinal Manifestations in Joint Hypermobility Syndromes. Am J Med Sci. 2018;355(6):573-80.

3. Colombi M, Dordoni C, Chiarelli N, Ritelli M. Differential diagnosis and diagnostic flow chart of joint hypermobility syndrome/ehlers-danlos syndrome hypermobility type compared to other heritable connective tissue disorders. Am J Med Genet C Semin Med Genet. 2015;169C(1):6-22.

4. Forghani I. Hypermobile Ehlers Danlos Syndrome. Balkan Med J. 2018.

5. Grahame R, Bird HA, Child A. The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). J Rheumatol. 2000;27(7):1777-9.

6. Malfait F, Francomano C, Byers P, Belmont J, Berglund B, Black J, et al. The 2017 international classification of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet. 2017;175(1):8-26.