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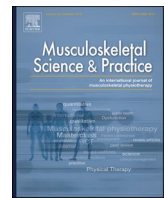
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Original article



Psychological factors and symptom duration are associated with exercise-based treatment effect in people with hypermobile shoulders: A secondary analysis of a randomised controlled trial

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ABSTRACT

Background: Shoulder symptoms are common in patients with hypermobility spectrum disorders (HSD), but few studies focus on identifying factors associated with treatment effects.

Aim: To identify baseline and clinical characteristics associated with a better outcome 16 weeks after starting an exercise-based treatment in patients with HSD and shoulder symptoms.

Design: Exploratory secondary analysis of data from a randomised controlled trial.

Method: Self-reported treatment outcome was reported as change between baseline and follow-up after 16 weeks of high-load or low-load shoulder strengthening. Multiple linear and logistic regressions were used to investigate associations of patient expectations of treatment effect, self-efficacy, fear of movement, and symptom duration with change in shoulder function, shoulder pain, quality of life, and patient reported health change. All regression models were performed firstly with adjustments for covariates (age, sex, body mass index, hand dominance, treatment group, and baseline score of the outcome variable) and secondly with additional adjustments for exposure variables.

Results: Expectations of complete recovery were associated with an increased odds of perceiving an important improvement in physical symptoms after a 16-week exercise-based treatment program. Higher self-efficacy at baseline seemed to be associated with improved shoulder function, shoulder pain and quality of life. A higher fear of movement seemed to be associated with increased shoulder pain and decreased quality of life. A longer symptom duration was associated with decreased quality of life.

Conclusion: Expectations of complete recovery, higher self-efficacy, lower fear of movement and shorter symptom duration seem to be important for better treatment outcomes.

1. Introduction

The term hypermobility spectrum disorder (HSD) was established in 2017 to diagnose people with symptomatic joint hypermobility (Castori et al., 2017). At least four of five people diagnosed with HSD experience shoulder symptoms (Palmer et al., 2017). Further, compared with the general population, people with HSD also report a higher occurrence of shoulder disability, high pain intensity, generalised pain, and reduced

health-related quality of life (Scheper et al., 2016; Kalisch et al., 2020; Johannessen et al., 2016). Often the recommended initial treatment for patients with HSD is exercise combined with passive modalities, and sometimes patients are offered surgical stabilisation of the joint (Warby et al., 2014, 2016; Engelbert et al., 2017). However, the evidence for both non-surgical and surgical treatment is weak, without consensus on standardised treatment (Warby et al., 2014, 2016; Palmer et al., 2014). Knowledge on the underlying mechanisms and factors associated with

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symptoms reported by patients with HSD is important, because it can support the development of optimal treatment (Johnson and Robinson, 2010; Malfait et al., 2021).

High quality clinical practice guidelines across various musculoskeletal disorders recommend the choice of treatment, among others, should be guided by an assessment of psycho-social factors to support the physical examination (Lin et al., 2020). However, only few studies have focused on the influence of psycho-social factors on the effect of exercise-based treatment in populations with shoulder disorders and uncertainty remains regarding the relevance of these factors with respect to treatment effect in patients with HSD and shoulder symptoms (Powell et al., 2022). Therefore, the proposed mechanism of exercise-based treatment effect for people with shoulder disorders, including populations with HSD and shoulder symptoms, is dominated by a biological explanation in clinical research (Warby et al., 2016; Powell et al., 2022).

A recent study by Chester et al. (2018) found psychological factors were consistently associated with outcomes from exercise-based treatment for people with shoulder pain in general, while clinical examination findings suggestive of a structural diagnosis were not (Chester et al., 2018). For example, patients with high expectations of recovery and high self-efficacy had better immediate and long-term treatment outcomes than patients with low expectations of recovery and low self-efficacy (Chester et al., 2018). Likewise, psychological traits like high levels of fear-avoidance beliefs have been reported to be associated with greater pain and disability, and a worse prognosis (Martinez-Calderon et al., 2018a, 2018b). However, since systematic reviews have reported equivocal results on the association between psychological factors and treatment outcomes in patients with shoulder disorders, firm conclusions cannot be drawn (Martinez-Calderon et al., 2018a, 2018b; Sheikhzadeh et al., 2021; De Baets et al., 2019). Of other potential factors associated with treatment effect, like symptom duration, the evidence is also inconclusive (Chester et al., 2018; Sheikhzadeh et al., 2021).

To our knowledge, no study has investigated the influence of psychological factors and symptom duration on exercise-based treatment outcome in a population with HSD and persistent shoulder symptoms. Therefore, the overall aim of this study was to investigate associations of patient expectations of treatment effect, self-efficacy, fear of movement, and symptom duration with change in shoulder function, shoulder pain, quality of life, and patient reported health change, after 16 weeks of exercise-based treatment.

2. Method

2.1. Study design

This is a secondary analysis of data from a randomised controlled trial (RCT) (Clinicaltrials.gov NCT03869307), comparing the effects of two different 16-week shoulder exercise programs in patients with HSD and shoulder symptoms for more than three months (Liaghat et al., 2022a). Data from baseline and 16-week follow-up from the RCT were included in this study. The study protocol for the RCT has been published in detail elsewhere (Liaghat et al., 2020) and information related to this study is summarised here. This study adhered to the STROBE guidelines (von Elm et al., 2007).

The data collection was approved as part of the trial from Regional Committees on Health Research Ethics for Southern Denmark (S-20170066). A statistical analysis plan (SAP) for this secondary analysis was registered with the Open Science Framework (<https://osf.io/s6yk4/>) prior to analysing the data.

2.2. Setting and participants

The RCT was conducted in primary care within the Region of Southern Denmark. From April 2019 to March 2021 patients were

recruited from their general practitioners and from 8 physiotherapy clinics. Patients were included if they met the following criteria for HSD: 1) Generalised joint hypermobility defined using the Beighton tests and the five-part questionnaire 2) Secondary musculoskeletal manifestations in the shoulder defined as chronic shoulder pain or mechanical shoulder symptoms (instability, subluxation, laxity) for at least 3 months without a history of trauma. Patients were excluded if they fulfilled any of the following: 1) Clinically suspected referred pain from the cervical spine 2) Diagnosis of systemic inflammatory rheumatic diseases, connective tissue diseases and/or neurological diseases 3) Pregnancy or childbirth within the past year or planning to get pregnant during the study period 4) Shoulder surgery within the past year 5) Steroid injection in the affected shoulder in the previous 3 months 6) Inability to speak or understand Danish 7) Inability to comply with the study protocol 8) Inability to provide informed consent (Liaghat et al., 2020, 2022a, 2022b). All patients had a medical referral to physiotherapy treatment because of their shoulder symptoms, and all provided written informed consent before participation in the RCT. The intervention consisted of 16 weeks of shoulder exercises (three sessions/week) with either HEAVY (full-range, high-load, supervised twice/week) or LIGHT (neutral/mid-range, low-load, supervised three times in total).

2.3. Data collection

During the enrolment process, general demographic information and the patients' expectations of treatment effect were collected by the principal investigator of the RCT (BL). Before starting the intervention, baseline anthropometric measures (and other objective measurements not used in this study) were collected by one of four blinded physiotherapists, at Esbjerg Municipality Rehabilitation Centre, Esbjerg, Denmark, or at the Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark. Patients completed self-reported outcome measures directly into the web-based Research Electronic Data Capture (REDCap) at baseline and after the intervention period, at the 16-week follow-up assessment. Both baseline and follow-up assessments were carried out in undisturbed rooms at the same locations, by the same blinded physiotherapists.

Before start of data collection, the four outcome assessors had received comprehensive education in the assessment protocol, during two sessions led by the principal investigator (BL), to agree on a standardised data collection procedure.

2.4. Exposure variables sampled at baseline

Patient expectations of treatment effect were assessed by asking the patients "How much do you expect your shoulder problem to change as a result of physiotherapy treatment?" and was measured on a 7-point Likert scale ranging from "0 - worse than ever" to "6 - complete recovery" (Chester et al., 2019). The patient expectations of treatment effect were dichotomised into 'high/low expectation', with expectations of 'complete recovery' defining 'high expectations', and expectations below 'complete recovery' defining 'low expectations'.

Self-efficacy related to symptoms was assessed using the Self-Efficacy Questionnaire. Self-efficacy was defined as the patients' beliefs in their ability to complete tasks and reach a desired outcome despite their shoulder symptoms. The total scores range from 0 to 60, where a higher score is equal to higher self-efficacy (Chester et al., 2019).

Fear of movement was assessed using Tampa Scale of Kinesiophobia-11 (TSK-11). The total scores range from 11 to 44, where a higher score is equal to higher fear of movement (Mintken et al., 2010).

Symptom duration was assessed during the enrolment process by asking the patients on symptom duration and it was measured in years from onset to enrolment.

2.5. Outcome variables sampled at baseline and 16-week follow-up

Shoulder function was measured using the total score of the Western Ontario Shoulder Instability Index (WOSI), using a validated Danish electronic version (Eshoj et al., 2017). The WOSI questionnaire is developed for patients with shoulder instability, has 21 questions, and covers four domains. Each question is scored on a visual analogue scale (VAS) ranging from 0 to 100, giving a total score of 0–2100. The best possible score is 0, equivalent to no shoulder-related limitation (Eshoj et al., 2017). The timeframe for WOSI is the past week.

Shoulder pain was measured using Numerical Pain Rating Scale (NPRS) with numbers from 0 to 10 (“no pain” to “worst pain imaginable”) (Breivik et al., 2008). The average pain level for the past 7 days was measured.

Health-related quality of life was assessed using European Quality of Life - 5 Dimensions - 5-Level Scale (EQ-5D-5L) index score. It is a classification system that comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), where each dimension is rated by a five-level ordinal scale as follows: (1) no problems, (2) slight problems, (3) moderate problems, (4) severe problems, and (5) extreme problems. The index scores range from -0.624 to 1, where full health equals 1 and dead equals 0 (Janssen et al., 2013; Jensen et al., 2021).

Global Perceived Effect (GPE) was measured at 16-week follow-up and used to assess patient reported health change on the ‘physical symptoms’ domain of the WOSI questionnaire. The patients rated their experienced change in relation to importance between baseline and 16-week follow-up assessments, on a 7-point scale ranging from “1 - worse, an important worsening” to “7 - better, an important improvement” (Kamper et al., 2010). The GPE was dichotomised as important improvement (points 6 and 7) and not important/worse (points 1 to 5).

2.6. Statistical analysis

The demographic and anthropometric variables, and the baseline scores of the self-reported exposure variables, were summarised using descriptive statistics. Shapiro-Wilk test and visual inspection of histograms and quantile-quantile plots (qq-plots) were used to check for normal distribution of continuous variables.

Effect was measured as change scores between baseline and follow-up after 16 weeks treatment and for GPE at 16-weeks follow-up, and baseline variables were used as covariates. The associations of the exposure variables (1) expectations of treatment effect, 2) self-efficacy, 3) fear of movement, and 4) symptom duration) with changes in the outcome variables (I) shoulder function, II) shoulder pain, and III) quality of life) were tested in multiple linear regression models. Change scores of the outcome variables were the dependent variables, and baseline scores of the exposure variables (and other covariates) were the independent variables. Each of the three outcome variables were tested in multiple linear regression models with one of the four exposure variables (and other covariates) at a time. To investigate the association of multiple exposure variables on the outcomes, three multiple regression models including all exposure variables (and other covariates) were performed.

The associations of the exposure variables (1) expectations of treatment effect, 2) self-efficacy, 3) fear of movement, and 4) symptom duration) and the dichotomised outcome variable patient reported health change (GPE) were tested in multiple logistic regression models. The dichotomised patient reported health change at 16-week follow-up was the dependent variable, and the baseline scores of the exposure variables (and other covariates) were the independent variables. Four multiple logistic regression models including one of the four exposure variables (and other covariates) at a time were performed. To investigate the association of multiple exposure variables on GPE, one multiple logistic regression model including all exposure variables (and other covariates) was performed.

All regression models were performed firstly with adjustments for covariates (age, sex, body mass index (BMI), hand dominance, treatment group, and baseline score of the outcome variable) and secondly with additional adjustments for all the investigated exposure variables, after investigating the risk of collinearity. Covariates were chosen a priori based on previous studies (Kjærbaek et al., 2022) and collinearity was investigated using the variance inflation factor. The analyses including adjustments for all exposure variables deviated from the SAP. A sensitivity analysis eliminating the baseline values of the other three of the analysed exposure variables patient expectations of treatment effect, self-efficacy, fear of movement, and symptom duration, based on the p-value, has been performed (supplementary file).

The assumptions for conducting linear regression (linearity, normal distribution, and constant variation of residuals) and logistic regression analyses (observed values matching expected values) were tested and met.

As this study was a secondary exploratory analysis of data from an RCT, no sample size calculations were performed. The level of significance was set at $p < 0.05$. All statistical analyses were performed with Stata (StataCorp. 2021. Stata Statistical Software: Release 17.0. College Station, TX: StataCorp LLC).

3. Results

Two hundred and seventy-nine patients were assessed for eligibility, of which 100 were included in the RCT (Liaghat et al., 2022a). All 100 patients delivered baseline data for this secondary analysis, and between 91 and 93 patients delivered data on the four outcomes at 16-week follow-up.

The majority were females (79%), and the mean age of all patients was 37.8 years (standard deviation (SD) 12.8) (Table 1). Approximately one fifth of the patients (18%) reported having had a previous shoulder dislocation, and almost half of the patients (48%) felt their shoulder was loose. Further, 68% of the patients reported having received previous shoulder treatment, of which 56 patients previously had visited a physiotherapist and received instruction in exercises for the shoulder without successful outcome.

The self-reported ‘expectations of treatment effect’ question was distributed with 92 of 100 patients answering the two highest possible scores, and none answering below expectations of ‘no improvement’, i.e. no patients answered the question with the three lowest scores.

Higher self-efficacy score at baseline was associated with improved shoulder function at follow-up (adjusted) (Table 2). Additionally adjusting for baseline self-efficacy, baseline fear of movement, symptom duration and expectations of treatment effect showed a trend towards an association between higher self-efficacy score at baseline and improved shoulder function at follow-up (Table 2).

Higher self-efficacy score at baseline was associated with a decrease in shoulder pain at follow-up (adjusted) (Table 3). Higher fear of movement score at baseline was associated with an increase in pain at follow-up (adjusted) (Table 3).

Higher self-efficacy score at baseline was associated with an increase in quality of life at follow-up (adjusted) (Table 4) and a higher fear of movement score at baseline was associated with a decrease in quality of life (adjusted) (Table 4). A longer symptom duration was associated with a decrease in quality of life (adjusted and adjusted for all exposure variables) (Table 4).

High expectations of treatment effect at baseline were associated with an increased odds of perceiving an important health improvement, WOSI ‘physical symptoms’ (adjusted and adjusted for all exposure variables) (Table 5).

4. Discussion

Higher self-efficacy at baseline was associated with improved shoulder function, shoulder pain and quality of life after a 16-week

Table 1

Baseline demographics, anthropometrics, and self-reported exposure variables in patients with HSD and persistent shoulder symptoms. Continuous variables are presented as mean and with standard deviation, and symptom duration as median and IQR. Categorical variables are presented as numbers/frequency and percentages.

Variable	All patients (n = 100)
Sex (female), (n, %)	79 (79)
Age (years)	37.8 (12.8)
Weight (kg)	80.3 (17.3)
Height (cm)	171.9 (9.0)
Body Mass Index (kg/m ²)	27.2 (5.6)
Dominant writing hand, right (n, %)	91 (91)
Symptomatic shoulder, right (n, %)	57 (57)
Previous shoulder dislocation, yes (n, %)	18 (18)
Feeling shoulder is loose, yes (n, %)	48 (48)
Educational level (n, %)	
Academic education	50 (50)
Skilled	28 (28)
Unskilled	5 (5)
No education	17 (17)
Employment status (n, %)	
Full-time	54 (54)
Part-time	10 (10)
Student	17 (17)
Unemployed/retired	11 (11)
Sick listed	8 (8)
Previous shoulder treatment, yes (n, %)	68 (68)
Exercise supervised by physiotherapist	56 (56)
Passive treatment delivered by physiotherapist	44 (44)
Chiropractic consultation	16 (16)
Prescribed analgesic medication	19 (19)
Other treatment (steroid injections, surgery)	21 (21)
Self-reported exposure variables	
Expectations of treatment effect (n, %)	
Complete recovery	41 (41)
Much improvement	51 (51)
Slight improvement	7 (7)
No improvement	1 (1)
Worse (3 options)	0 (0)
Self-efficacy score, 0-60	44.9 (10.4)
Fear of movement score, 11-44	22.7 (5.5)
Symptom duration, years	3.3 (1-8)

exercise-based treatment program. A higher fear of movement was associated with increased shoulder pain and decreased quality of life. A longer symptom duration was associated with decreased quality of life, and high expectations of treatment effect was associated with an increased odds of perceiving an important positive change in physical symptoms. However, only the association between symptom duration and quality of life, and the association between expectations of treatment effect and perceiving an important positive change in physical symptoms, were statistically significant after adjustment for all exposure variables.

Self-efficacy was the variable associated with change on most outcomes, with high levels of self-efficacy being associated with increased treatment effect on shoulder function, shoulder pain, and quality of life.

These results align with previous literature reporting an association between high levels of self-efficacy and reduced pain intensity and increased function, in populations with shoulder pain or chronic shoulder pain (Martinez-Calderon et al., 2018a, 2018b; De Baets et al., 2019).

Even though high expectations of treatment effect were associated with an increased odds of perceiving an important improvement in physical symptoms, measured on the GPE scale, no increased treatment effects on shoulder function or pain were demonstrated. This contrasts with the findings of three recent systematic reviews, investigating the role of psychological factors on pain and disability in patients with shoulder pain or chronic shoulder pain (Martinez-Calderon et al., 2018a, 2018b; De Baets et al., 2019). However, different cut-points for defining

Table 2

Associations between baseline expectations of treatment effect, self-efficacy, fear of movement, and symptom duration with change in shoulder function (total WOSI-score) in patients with HSD and persistent shoulder symptoms (n = 93).

	Adjusted ^a			Adjusted for exposure variables ^b		
	Beta- coefficient	95% CI	R ²	Beta- coefficient	95% CI	R ² 0.31
Expectations of treatment effect						
Low	Reference			Reference		
High	-91.1	-245.9, 63.8	0.27	-75.4	-234.0, 83.2	
Self-efficacy	-9.5	-18.6, -0.42	0.30	-7.9	-17.8, 2.0	
Fear of movement	13.4	-1.1, 27.8	0.29	7.07	-9.1, 23.3	
Symptom duration	0.60	-9.7, 10.9	0.26	-0.41	-10.5, 9.7	

WOSI: Western Ontario Shoulder Instability Index. CI: Confidence Interval. HSD: Hypermobility Spectrum Disorder.

^a Adjusted for age, sex, body mass index (BMI), hand dominance, treatment group and baseline WOSI-score.

^b Adjusted for baseline self-efficacy, baseline fear of movement, symptom duration, expectations of treatment effect, age, sex, BMI, hand dominance, treatment group and baseline WOSI-score.

Table 3

Associations between baseline expectations of treatment effect, self-efficacy, fear of movement and symptom duration with change in shoulder pain (NPRS) in patients with HSD and persistent shoulder symptoms (n = 92).

	Adjusted ^a			Adjusted for exposure variables ^b		
	Beta- coefficient	95% CI	R ²	Beta- coefficient	95% CI	R ² 0.41
Expectations of treatment effect						
Low	Reference			Reference		
High	-0.64	-1.4, 0.086	0.37	-0.50	-1.2, 0.25	
Self-efficacy	-0.046	-0.87, -0.0053	0.38	-0.034	-0.081, 0.012	
Fear of movement	0.070	0.0043, 0.14	0.38	0.031	-0.046, 0.11	
Symptom duration	0.013	-0.035, 0.062	0.35	0.0034	-0.044, 0.051	

NPRS: Numerical Pain Rating Scale. CI: Confidence Interval. HSD: Hypermobility Spectrum Disorder.

^a Adjusted for age, sex, body mass index (BMI), hand dominance, treatment group and baseline NPRS score.

^b Adjusted for baseline self-efficacy, baseline fear of movement, symptom duration, expectations of treatment effect, age, sex, BMI, hand dominance, treatment group and baseline NPRS score.

Table 4

Associations between baseline expectations of treatment effect, self-efficacy, fear of movement and symptom duration with change in quality of life (EQ-5D-5L) in patients with HSD and persistent shoulder symptoms (n = 91).

	Adjusted ^a			Adjusted for exposure variables ^b		
	Beta- coefficient	95% CI	R ²	Beta- coefficient	95% CI	R ² 0.52
Expectations of treatment effect						
Low	Reference			Reference		
High	0.039	-0.009, 0.088	0.43	0.024	-0.022, 0.071	
Self-efficacy	0.003	0.0004, 0.005	0.44	0.002	-0.0001, 0.004	
Fear of movement	-0.006	-0.010, -0.002	0.46	-0.004	-0.009, 0.001	
Symptom duration	-0.005	-0.008, -0.002	0.47	-0.004	-0.007, -0.001	

EQ-5D-5L: European Quality of life-5 Dimensions-5-Level Scale. CI: Confidence Interval. HSD: Hypermobility Spectrum Disorder.

^a Adjusted for age, sex, body mass index (BMI), hand dominance, treatment group and baseline EQ-5D-5L score.

^b Adjusted for baseline self-efficacy, baseline fear of movement, symptom duration, expectations of treatment effect, age, sex, BMI, hand dominance, treatment group and baseline EQ-5D-5L score.

Table 5

Associations between baseline expectations of treatment effect, self-efficacy, fear of movement and symptom duration, with patient reported health change (GPE on 'physical symptoms' in WOSI) in patients with HSD and persistent shoulder symptoms (n = 92).

	Adjusted ^a		Adjusted for exposure variables ^b	
	OR	95% CI	OR	95% CI
Expectations of treatment effect				
Low	Reference		Reference	
High	3.2	1.2, 8.7	2.9	1.005, 8.3
Self-efficacy	1.00	0.96, 1.05	0.99	0.94, 1.04
Fear of movement	0.95	0.87, 1.04	0.97	0.87, 1.08
Symptom duration	0.97	0.90, 1.05	0.98	0.90, 1.06

GPE: Global Perceived Effect. CI: Confidence Interval. HSD: Hypermobility Spectrum Disorder.

^a Adjusted for age, sex, body mass index (BMI), hand dominance and treatment group.

^b Adjusted for baseline self-efficacy, baseline fear of movement, symptom duration, expectations of treatment effect, age, sex, BMI, hand dominance and treatment group.

'high/low expectations' may be a reason for this difference. The study by [Chester et al. \(2018\)](#), included in all three above-mentioned reviews, used a lower cut-point for high 'expectations of treatment effect' when demonstrating an association with better outcomes of shoulder function and pain. However, we were not able to use a lower cut-point in this study, since most patients reported high expectations, with 92 of 100 answers distributed on the two highest scores of seven possible.

Fear of movement is a common trait in people with HSD and may be a major problem for some people in this population ([Liaghat et al., 2022b](#); [Mintken et al., 2010](#)). The association between higher levels of fear of movement and decreased treatment effect on pain in our study is in line with a systematic review, investigating the role of psychological factors on pain intensity and disability in patients with chronic shoulder

pain undergoing conservative/non-surgical treatment ([Martinez-Calderon et al., 2018b](#)). However, this contrasts with other systematic reviews on patients with shoulder pain, reporting either no association between baseline fear of movement and pain, or inconsistency of the association between fear of movement and pain in patients receiving conservative treatment ([Martinez-Calderon et al., 2018a](#); [Sheikhzadeh et al., 2021](#); [De Baets et al., 2019](#)). When comparing these findings on the association between fear of movement and pain with our result, it is important to emphasise the apparent differences between the studies. The systematic review by [De Baets et al. \(2019\)](#), reporting no association between baseline fear of movement and pain, concluded based on two studies; Both studies used The Fear-Avoidance Beliefs Questionnaire for assessing fear of movement, but in different patient populations (subacromial pain and rotator cuff tears) and with no standardised treatment intervention, and this may explain the contrasts in results from the present study. In line with two recent systematic reviews, we did not find an association between baseline fear of movement and treatment effect on shoulder function ([Martinez-Calderon et al., 2018b](#); [De Baets et al., 2019](#)). However, this contrasts with the findings by [Martinez et al. \(2018\)](#) who found higher levels of fear of movement at baseline to predict greater shoulder disability overtime ([Martinez-Calderon et al., 2018a](#)). Although our adjusted analyses showed an association between baseline fear of movement with shoulder pain and quality of life, the analyses may have been underpowered to detect an association with shoulder function. Further, in the analyses adjusted for the exposure variables the correlation between the exposure variables may have affected the model to estimate weaker associations with the outcome variable.

4.1. Implication for clinical practice

Increased knowledge on the association of psychological factors and exercise-based treatment effect in patients with HSD and shoulder

symptoms may help guiding clinicians to deliver higher quality treatment. The three multiple regression models adjusted for exposure variables showed R-squared values between 0.31 and 0.52, meaning the models explained up to approximately 50% of the variance. Therefore, variables not included in the current models may influence the investigated associations. However, our findings support identifying and addressing low expectations, low self-efficacy, and high fear of movement as part of the treatment plan. In addition, the findings suggest that despite long symptom duration, positive treatment effects seem still to be achievable. However, longer symptom duration could result in psychological distress and poorer health outcomes (e.g. quality of life) that should be taken care of. Further, even moderate symptoms and disability experienced over long time may have substantial impact on overall wellbeing (Ackerman et al., 2022). Although our findings suggest the investigated psychological factors may be associated with treatment outcome, this study does not address how the investigated psychological factors should be targeted in combination with exercise-based treatment. However, psychological interventions delivered by physiotherapists, combined with exercise have shown promising results to improve health outcomes in musculoskeletal pain conditions in general (Silva Guerrero et al., 2018).

Since this is one of the first studies to investigate factors associated with exercise-based treatment effect in a population with HSD and persistent shoulder symptoms, the results are primarily generalisable to similar patient groups in a primary care setting, but not necessarily generalisable to patients in secondary care and patients with hypermobile Ehlers-Danlos Syndrome. Due to the limited number of studies on this patient group, future research is needed to investigate the association between psychological factors and treatment effect to support our findings.

4.2. Limitations and strengths

A methodological limitation when carrying out secondary analyses of data from an RCT is the lack of a comparison group and the question of causality. Furthermore, the original RCT was powered to detect a treatment effect on the total WOSI-score, rather than the association of exposure variables with treatment effect. Along this line, a limitation was the limited distribution of the patients' expectations of treatment effect, which decreased the power to detect an association between 'expectations of treatment effect' and the four outcomes. The sample may not represent the full population of interest as most of the participants had high expectations to the treatment. On the other hand, participants had experienced shoulder pain for a long time and prior treatment had shown minor or no effect. Further, the selected exposure variables were only a limited sample of many biopsychosocial factors that potentially may be associated with the effect of exercise-based treatment (Engebretsen et al., 2010; Struyf et al., 2016).

A strength of the study was the preparation and online registration of a statistical analysis plan prior to conducting the analyses (<https://osf.io/s6yk4/>), reducing confirmation and publication bias. In addition, the use of patient reported outcome measures, which are reliable, valid, and responsive in populations with shoulder instability and/or shoulder pain, increased the internal validity (Mintken et al., 2009, 2010; Eshoj et al., 2017; Kirkley et al., 1998).

5. Conclusion

In patients with HSD and persistent shoulder symptoms from Danish primary care, expectations of complete recovery, higher self-efficacy, lower fear of movement and shorter symptom duration seem to be important for better treatment outcomes after 16 weeks of exercise-based treatment.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.msksp.2023.102798>.

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