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Title: A Cluster of High Psychological and Somatic Symptoms in Children with Idiopathic Scoliosis Predicts Persistent Pain and Analgesic Use One Year after Spine Fusion

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- **What is already known:** Persistent postoperative pain occurs in one of five children undergoing major surgery, yet factors associated with this are uncertain.
- **What this paper adds:** Children exhibiting a cluster of psychological and somatic symptoms, suggesting a pain vulnerable trait preoperatively, report worse pain outcomes one year after spine fusion.

Abstract

Background: Persistent postoperative pain is a significant problem for many children, particularly for those undergoing major surgery such as posterior spine fusion. More than two-thirds report persistent pain after spine fusion, yet factors that may contribute to poorer outcomes remain poorly understood.

Aim: This prospective, longitudinal study examined how psychologic and somatic symptoms cluster together in children aged 10 to 17 years with idiopathic scoliosis, and tested the hypothesis that a higher psychological and somatic symptom cluster would predict worse pain outcomes one year after fusion.

Methods: Otherwise healthy children with idiopathic scoliosis completed preoperative surveys measuring recent pain intensity, pain location(s), somatic symptom severity, painDETECT (neuropathic-type pain symptoms), pain interference, fatigue, depression, anxiety, and pain catastrophizing. Pain outcome data were collected during hospitalization, and at one year after surgery.

Results: Ninety-five children completed baseline surveys and a cluster analysis differentiated 28 (30%) with a high symptom profile that included; higher depression, fatigue, pain interference, catastrophizing and painDETECT scores. High symptom cluster membership independently predicted higher pain interference at one year (β 9.92 [95% CI 6.63, 13.2], $p < 0.001$). Further, children in this high symptom cluster reported significantly higher pain intensity and painDETECT scores, and had a 50% higher probability of continued analgesic use at one year compared to those in the Low Symptom Cluster (95% CI 21.3 - 78.5, $p = 0.001$).

Conclusions: Findings from this exploratory study suggest a need to comprehensively assess children with scoliosis for preoperative signs and symptoms that may indicate an underlying vulnerability for persistent pain. This, in turn may help guide a comprehensive perioperative treatment strategy to mitigate the potential for long-term pain trajectories.

Key Words: children, adolescents, pediatric pain, chronic pain, musculoskeletal pain, postoperative pain

Persistent postoperative pain poses a significant healthcare problem for many children and adolescents. Thirteen to 22% of children report persistent pain 6-12 months after major surgery,¹⁻³ with one third reporting daily pain and 14%, severe pain.² Lower rates (5%) are reported following less invasive outpatient procedures,⁴ while highest rates (up to 75%) are found following posterior spine fusion.^{5,6} Longitudinal studies have described moderate to severe pain in nearly one third of children with idiopathic scoliosis that remained unimproved or worsened for 16% for up to 5 years after surgical correction.^{5,7,8} Importantly, no obvious nociceptive source for pain could be identified in 85% of children with persistent pain after

fusion.⁹ Furthermore, the degree and location of curve, surgical approach, fusion length, and magnitudes of correction correlate poorly or not at all with persistent pain, and removal of hardware after 2 years did not relieve pain for 40% of children with severe pain.^{5,7,8,10} Such data suggest that non-nociceptive factors may better explain persistent pain after surgery.

Despite the high prevalence and potential negative impact of persistent postoperative pain in children, risk factors remain poorly understood. Several studies in small samples of children suggest that child parental psychosocial factors help to explain persistent pain after major surgery.^{11,12} However, as summarized in a recent systematic review, variations in study methods and sample characteristics limit the interpretation of data and call for further study.³ On the other hand, this growing body of evidence suggests that a significant portion of children with scoliosis exhibit characteristics prior to surgery that indicate a particular vulnerability for a long term pain trajectory. Such factors include, pain presence and severity, anxiety sensitivity, poorer coping, negative mood, higher analgesic use and simple markers of functioning such as missed school days.^{5-7,9} We recently described a cluster of self-reported psychological and somatic symptoms that was present in 30% of those with idiopathic scoliosis prior to surgery.¹³ These symptoms included higher depression, fatigue, multi-site pain and somatic symptomatology, neuropathic pain symptoms, pain interference and pain catastrophizing. Furthermore, children with this cluster of symptoms experienced higher pain and analgesic use in the immediate two-weeks following surgery. We postulated that this symptom cluster may be related to the same phenomenon commonly seen in subsets of adults with chronic pain and indicative of greater central nervous system contributions to pain (i.e., central pain sensitization or augmentation).¹⁴ These and other investigators have argued that the phenotype associated with chronic postoperative pain is similar to that found in patients with centralized pain sensitization which, in turn, is supported by demonstrated differences in quantitative sensory testing and neuroimaging.¹⁴

The present study continued our earlier exploratory work with the aim to determine whether children who self-report a cluster of higher psychological and somatic symptoms would remain vulnerable to persistent postoperative pain one year following posterior spine fusion. Specifically, we tested the following hypotheses: 1) Children with higher psychological and somatic symptomatology prior to surgery would report higher pain and pain interference one year after posterior spine fusion; 2) These high risk children would also be more likely to need ongoing analgesic use at one year.

Methods

With approval from the institutional review board at the University of Michigan and written parental consent and child assent, we consecutively recruited cognitively intact, English-speaking children aged 10 to 17 years scheduled to undergo primary elective posterior spine fusion for surgical correction of idiopathic scoliosis from July 2014 to December 2016. We excluded those who had previous spine surgery and those with cognitive impairments who could not independently complete surveys. One-year follow-up concluded in Jan 2018. The study design was a prospective, longitudinal observational study.

Measures:

Pain Intensity was self-reported by participants with the 0-10 Numeric rating scale (NRS) where 0 = no pain and 10 = “worst pain possible”.¹⁵

Pediatric Fibromyalgia Survey Criteria (pFSC) combines scores from the two-sided body map (i.e., child’s self-reported pain locations) and a modified Somatic Symptom Severity tool (child’s global perceptions of somatic symptoms) to identify widespread pain and symptoms common in children and adults with centralized pain conditions such as fibromyalgia (score range 0-31).^{16,17} A similar version of the fibromyalgia survey criteria was recently found to have excellent sensitivity and specificity for diagnosing juvenile fibromyalgia in adolescents.¹⁷ Scores from our pFSC were found to be reliable in this age group (ICC 0.912 [95% CI 0.845-0.95]) and helped to differentiate symptom clusters in our previous work.¹³ Scores range from 0 to 31 and are treated as continuous to reflect what is now considered to be a continuum of pain centralization.¹⁸

Widespread pain was defined as pain in three or more regions of the body as identified on the self-reported body map and as defined previously.¹⁹

painDETECT documented the presence and extent of neuropathic-type pain symptoms with scores ranging from 0 to 39. We previously demonstrated that this measure has good internal consistency (Cronbach α 0.757 [95% CI 0.662-0.834]) and “test-retest” reliability (ICC 0.77 [95% CI 0.365-0.811]) in this age group.¹³

Pediatric Patient-Reported Outcome Measurement System (PROMIS) Short Forms were used to measure somatic and psychologic symptoms including, fatigue, depression, anxiety, and pain interference. These measures have been found to have good reliability in children and yield scores ranging from 0 to 32 (pain interference, depression, anxiety) or 0-40 (fatigue).^{20,21}

Pain Catastrophizing measures the degree of “pain worry” in children. Scores range from 0 to 52, and the instrument has excellent psychometric properties and predictive validity.²²

Procedures:

Following parental consent and child assent in the preoperative clinic, children independently completed the baseline surveys using an iPad with a Qualtrics link. The surveys

included automatic reminder messages for missing items in order to encourage complete responses and reduce missing data. The survey contained only a unique identifier to ensure privacy and honest disclosure. Approximately two weeks after the clinic visit, children underwent posterior spine fusion and we recorded the child's demographics, surgical information, and all analgesics administered (opioids were converted to oral morphine equivalents per kilogram per hour of hospital stay). Children were visited each day in the hospital to obtain self-reported pain intensity scores. One year after surgery, children completed a paper follow-up survey (in person at the follow-up clinic visit or by mail) regarding recent and current pain presence, intensity, pain interference, neuropathic pain symptoms, and analgesic use.

Statistical Analyses

Missing data were minimal (<3 items for the baseline depression survey in two children). These missing items were imputed from the average of the completed depression items. We used SPSS (version 24) to analyze all data. Pain measures and surveys were considered continuous measures and summarized with descriptive statistics as means \pm standard deviations (SD), and medians (M) with percentiles, where applicable and based on tests of normality. Nominal data are reported as n (%).

We first conducted a series of two-step cluster analyses which uses a log-likelihood distance measure to differentiate or profile children based on the ideal number of homogeneous structures suggested by the data, and not defined a priori. The two-step is robust to violations in assumptions of independence and normality, and, for these analyses, the Akaike information criterion was chosen as the clustering criterion. Our models included all of the baseline symptom variables of interest (i.e., PROMIS depression, anxiety, and pain interference, painDETECT, pain catastrophizing, and pFSC) since these were deemed to measure relevant and non-redundant attributes (i.e. all correlations $< 0.76^{23}$). We subsequently removed the non-contributing factors (i.e., non-significant or $p < 0.05$) anxiety and pFSC, until a final solution with a high measure of cohesion was obtained. The resultant cluster groups of children were compared with univariate analyses (chi square, unpaired t or Mann Whitney U tests) with regard to; demographics, preoperative factors, surgical course, and one-year pain outcomes. Mean differences (MD) or odds ratios (OR) with 95% confidence intervals (CI) are reported. We then tested the hypotheses using multivariable linear regression for the outcome, Pain Interference and a mixed effect logistic regression for the outcome, ongoing analgesic use. The following covariates were included in the models together with the primary factor of interest, cluster membership: age, sex, body mass index, spine levels fused, intraoperative analgesic technique (i.e., intrathecal vs. other), average in-hospital NRS score, and total morphine consumption.

We recruited 100 children to obtain a sample large enough to estimate a 20% proportion with multi-site pain and symptomology (95% CI = 0.20), allowing for an estimated 25% loss-to-follow up. The resultant sample (n=75) was determined, a priori, to be more than sufficient to include up to 6 variables in a two-step cluster analysis (recommended 2^k),²⁴ and to detect at least a 40% difference in analgesic requirement (i.e., the smallest expected effect size) at one year ($\alpha = 0.05$; $\beta = 0.20$).

Results

One hundred twenty-seven children were approached for this study, and 23 declined participation or did not meet inclusion criteria. One-hundred four children were enrolled, however, we excluded 3 due to surgical variation or secondary spine fusion, 2 who could not independently complete baseline surveys, and 4 who had surgery postponed or cancelled. Ninety-five children completed all baseline surveys and underwent surgery. The final cluster analyses differentiated two groups with a high degree of separation and cohesion. Figure 1 depicts, in order of contribution, the psychological and somatic symptom scores that best differentiated a High Symptom Cluster of children (prevalence = 28 [95% CI 22 to 38]) from a Low Symptom Cluster of children. Table 1 describes the baseline characteristics and the surgical/hospital course of children in these clusters. In addition to the cluster factor differences, children in the High Symptom Cluster reported higher preoperative pain intensity, anxiety and pFSC scores, were more likely to report widespread pain and to have been using analgesics compared with children in the Low Symptom Cluster. These children also reported higher pain intensity during their hospital stay, but used similar amounts and types of analgesics postoperatively.

Seventy-six children (80% of those recruited) completed all parts of the one-year follow-up survey, and nearly all of these did so in person at their one-year clinic visit. The 20% lost to follow-up were excluded from the longitudinal analyses. The group lost to follow-up, however, was not different from children who completed the 1 year follow-up with regard to female sex (68% vs. 78%, $p=0.402$), age (14.5 vs. 13.9 yrs, $p=0.255$), body mass index (23.1 vs. 21.7 kg/m², $p=0.301$), baseline scores on catastrophizing (11.9 v 11.6, $p=0.907$), PROMIS depression (8.3 vs. 5.5, $p=0.158$), fatigue (10.1 vs. 8.2, $p=0.385$), anxiety (10.6 vs. 11.7, $p=0.646$), painDETECT (4.3 vs. 4.9, $p=0.668$), or baseline presence of widespread pain (26% vs. 29%, $p=0.820$).

The High Symptom Cluster reported significantly higher pain intensity, pain interference, and neuropathic-type pain and were more likely to be taking analgesics (primarily over-the-counter non-opioids) and using non-pharmacologic pain (primarily acupuncture [20%]) and

meditation [17%]) treatments at one year (see Table 2). Additionally, the pain outcomes were highly correlated with rho coefficients ranging from 0.598 to 0.785, $p < 0.01$. When adjusted for other baseline characteristics and hospital course variables, Cluster Membership independently predicted pain interference scores ($\beta = 9.92$ [95% CI 6.63, 13.2], $p < 0.001$; see Table 3). The mixed effect logistic regression model demonstrated that, adjusted for mean values of all baseline characteristics and hospital course variables, children in the High Symptom Cluster had a 50% higher probability of continued analgesic use at one year compared to those in the Low Symptom Cluster (estimated marginal mean = 50% [95% Confidence Interval = 21.3, 78.5], $p = 0.001$).

Of note, while children in the High Symptom Cluster had higher ongoing pain and pain interference at one year, they did experience a significant decrease in reported PROMIS pain interference from their baseline scores (MD -5.65 [95% CI 2.6, 8.7] paired t $p = 0.001$). In contrast, pain interference scores in the Low Symptom Cluster were no different from baseline (MD 0.85 [95% CI -0.47, 2.18] $p = 0.20$).

Discussion

Findings from this longitudinal study suggest that 30% of children with idiopathic scoliosis can be differentiated by a high degree of psychological and somatic symptomatology prior to surgery including; higher depression, pain interference, pain catastrophizing, fatigue, and neuropathic-type pain symptoms. Children with this cluster of symptoms reported significantly greater pain interference and were 50% more likely to be taking analgesics (primarily non-opioids) one year after posterior spine fusion. These data suggest that, even before surgery a pain vulnerable profile that predicts the observed long-term postoperative trajectory can be identified in children with scoliosis who require posterior spine fusion.

Importantly, children in the Low and High Symptom Cluster groups did not differ with regard to surgical characteristics, perioperative and hospital management, and these factors were not independently associated with long-term outcomes. We did find, however, that the High Symptom Cluster reported higher pain intensity after surgery and at one year. Unlike previous data,¹² we and others⁴ did not find an association between postoperative pain intensity scores and persistent pain. This discrepancy in findings may be due to the presence and stronger predictive value of the baseline cluster of psychological and somatic symptoms (i.e., depression, fatigue, pain worry, neuropathic-like symptoms). Others have similarly found strong and independent associations between psychological characteristics such as “anxiety sensitivity”,^{12,25} child pain catastrophizing²⁶ and long-term postoperative pain outcomes. Our data provide a more comprehensive description of the psychological and somatic characteristics

that may cluster together to predict long term pain trajectories after surgery. As such, findings suggest a need to characterize symptomology in children with idiopathic scoliosis before surgery, and to initiate symptom reduction strategies before and immediately after posterior spine fusion. Targeted interventions might include psychologic, non-pharmacologic and, possibly pharmacologic strategies to reduce depression symptoms, promote sleep and coping capacity, and relieve symptoms of neuropathic-type of pain.

Emerging evidence of multi-site and symptom clusters across differing chronic and recurrent pain syndromes in children suggest that they may not be separate disorders, but rather early manifestations of an underlying pain phenotype that persists into adulthood. Clusters of symptoms that include depression, anxiety, and daytime fatigue have been described in children with chronic musculoskeletal and other pain conditions and have been correlated with poorer functioning.^{27,28} Higher levels of somatization, depression and symptom internalization scores were found to predict persistent or recurrent pain trajectories in large community samples of children.^{29,30} These and other data suggest a “pain vulnerable” trait that emerges during childhood and that may reflect, in part, a neurobiological mechanism such as central pain sensitization or augmentation.³⁰ Recent data correlating higher catecholamine levels in cerebrospinal fluid preoperatively with persistent pain 6 weeks after spine fusion suggest a potential underlying mechanism for pain sensitization.³¹ However, this study also found an association with elevated systemic catecholamine levels, and thus, a central mechanism for persistent pain remains hypothetical. Other reports ruled out physiologic or nociceptive causes for 65% of patients who reported persistent pain 23 years after adolescent spine fusion.³² Importantly, in the present study, fibromyalgia survey criteria scores did not contribute to cluster membership in our study, but were significantly higher at baseline for children in the High Symptom Cluster (mean 10.93 vs. 5.69 for the Low Symptom Cluster). These average scores in our high symptom group are lower than the reported total cut-point for a diagnosis of fibromyalgia (i.e., ≥ 13), however, it has been suggested that central pain sensitization is a continuum, and that survey criteria scores provide a global conceptualization of this continuum.¹⁸ Whether higher pFSC scores indicate the early stages of pain sensitization is unclear from our findings. Further study that includes quantitative sensory testing in conjunction with our baseline measures is needed to better understand whether pain sensitization is a potential mechanism for persistent postoperative pain in children with scoliosis.

It is important to note that although we found ongoing pain outcome differences between the High and Low Symptom Clusters, children in the High Symptom Cluster did experience a decrease in their pain interference scores from baseline. This is somewhat similar to a recent

longitudinal study demonstrating that among adolescents who reported higher pain at baseline, most reported improvements 1-5 years after surgery.⁷ This study also found that children whose pain improved had reported lower body image at baseline compared to children who experienced a worsening pain trajectory. The investigators suggested that improved overall body image following surgical correction of scoliosis may help to explain an improved long-term pain outcome.

The ability to generalize findings from this study is limited by the potential for symptom recall which could have biased the self-report of symptomology prior to surgery. However, we previously reported the stability of self-reported scores from the clinic visit to approximately two-weeks later, supporting the reliability of recall in this age group. The contributions of various symptom measures to cluster membership differed slightly from our previous and smaller sample. The strong contributions of depression, catastrophizing, pain interference and fatigue to cluster membership remained stable from our earlier study, whereas pFSC no longer helped to differentiate the children. However, the criterion validity of our resultant clusters was supported by the demonstrated differences between clusters in the theoretically related baseline variables, pain intensity and widespread pain. It will be important to examine whether similar symptom clusters can be differentiated and validated in larger and varied samples of children and whether the predictive value of a high symptom cluster remains important when controlled for other factors such as parental psychological measures. Lastly, 20% of our sample was lost to follow-up which could have biased our results. However, the characteristics of those children were similar to those who completed the one-year follow-up, reducing the potential for non-response bias.

Findings from this exploratory study suggest that children with idiopathic scoliosis can be differentiated prior to undergoing posterior spine fusion by a cluster of symptomology that indicate vulnerability to a long-term pain trajectory. It is important to identify such pain vulnerable children before surgery so that a comprehensive plan of care might be initiated and individualized in a cost-efficient manner. This, in turn, could help to mitigate the potential negative impact that persistent postoperative pain can have on children's day-to-day physical and social functioning and quality of life.

Disclosures:

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Table 1. Baseline and Surgical Course Characteristics of the Cluster Profile Groups

Baseline Characteristics	Low Symptom Cluster (n=67)	High Symptom Cluster (n=28)	MD or OR [95% CI], p value
Age (range 10-17 years, both groups)	14.03 ± 1.73	14.11 ± 1.97	0.08 [-0.73, 0.88], 0.849
Weight (kg)	57.01 ± 13.38	63.12 ± 16.54	6.1 [-0.31, 12.5], 0.062
Body mass index	21.22 ± 4.93	23.80 ± 5.27	2.6 [0.33, 4.83], 0.025
Female Sex	48 (72%)	24 (86%)	0.42 [0.13, 1.38], 0.192
ASA Class 1-2 (vs. 3)	64 (96%)	25 (89%)	0.39 [0.07, 2.07], 0.355
Worst recent pain intensity (NRS 0-10)	3.9 ± 2.7	6.8 ± 2.0	2.82 [1.72, 3.9], <0.001

Widespread pain	15 (22%)	12 (43%)	0.39 [0.15, 0.99], 0.044
PROMIS Anxiety scores	9.52 ± 8.60	16.11 ± 7.42	-6.58 [-10.28, -2.89] 0.001
Fibromyalgia survey criteria	5.69 ± 4.8	10.93 ± 4.0	-5.24 [-7.28, -3.20] <0.001
Recent Analgesic Use	45 (67%)	27 (96%)	0.08 [0.01, 0.59], 0.002
[Opioid use]	[n=0]	[n=3]	
Recent non-pharmacologic use	35 (52%)	20 (71%)	0.44 [0.17, 1.13], 0.084
	Low Symptom Cluster (n=67)	High Symptom Cluster (n=28)	MD or OR [95% CI], p value
Perioperative Analgesia Method			
Epidural	12 (18%)	5 (18%)	
Intrathecal morphine	50 (75%)	22 (79%)	0.80 [0.28, 2.31], 0.682
IV PCA	5 (8%)	1 (4%)	
Hospital morphine consumption (mg/kg/hr)^a	0.08 ± 0.06	0.07 ± 0.05	-0.01 [-0.04, 0.01], 0.613 ^b
Average pain in hospital (0-10 NRS)	4.6 ± 1.7 (M 4.6)	5.7 ± 1.8 (M 5.9)	1.10 [0.34, 1.86], 0.012 ^b
Number of spinal levels fused	Median 11 Range [6-15]	Median 10 Range [7-14]	-0.57 [-1.4, 0.28], 0.136 ^b
Thoracic segments only	14 (20.9%)	7 (25.0%)	1.26 [0.45, 3.57], 0.660
Thoracic and lumbar	53 (79.1%)	21 (75.0%)	
Anesthesia duration (hrs)	5.9 ± 1.2	5.4 ± 1.1	-0.50 [-1.01, 0.01], 0.056
Hospital length of stay (hrs)	73.7 ± 20.2	75.0 ± 13.0	1.3 [-6.9, 9.5], 0.758

Data are presented as mean ± standard deviation or as n (%), where applicable. MD=Mean Difference; OR=Odds Ratio; CI=Confidence Interval; M=Median, IVPCA=Intravenous Patient Controlled Analgesia; NRS=Numeric Rating Scale; ^a All opioids converted to morphine equivalents for this variable; ^bMann Whitney U test of significance for non-parametric data

Table 2. Description of the Long Term Outcomes in the Cluster Profile Groups

	Low Symptom Cluster (n=56)	High Symptom Cluster (n=20)	MD or OR [95% CI], p value
Recent high pain score (range 0-10)	2.07 ± 2.0 M=1	4.8 ± 2.5 M=1	2.73 [1.4, 4.0], <0.001 ^c
PROMIS Pain Interference (range 0-	3.38 ± 5.0	11.05 ± 6.74	7.67 [4.3, 11.1], <0.001
PainDETECT	3.86 ± 4.21	9.76 ± 7.08	5.90 [2.1, 9.7], 0.004
Fibromyalgia Survey Criteria	4.16 ± 3.18	8.26 ± 4.39	-4.10 [-6.35, -1.86], 0.001
Analgesic use ^a	27 (48%)	18 (90%)	0.10 [0.02, 0.49], 0.001
Non-pharmacologic pain relieving methods used ^b	24 (43%)	15 (75%)	0.25 [0.08, 0.78], 0.014
Median number of healthcare visits in the year	5 [IQR 3, 7]	4 [IQR 3, 6]	P = 0.358 ^c

Data are presented as mean ± standard deviation or as n (%), where applicable.

MD=Mean Difference; OR=Odds Ratio; CI=Confidence Interval; M=Median; PROMIS= Patient Reported Outcome Measurement Information System; ^aReported analgesics were all over-the-counter non-opioids except for 1 in the Low Symptom group that used tramadol, 1 in the High Symptom group using oxycodone and another in the High Symptom group using tizanidine.

^bIncludes heat/ice, meditation, acupressure, acupuncture, physical therapy, other.

^cMann Whitney U test of significance.

Table 3. Associations between Baseline Characteristics and Long-Term Pain Interference Scores based on the Multivariable Regression Analysis

	β [95% Confidence Interval]	P Value
Age (years)	0.39 [-0.38, 1.16]	0.315
Body mass index (kg/m²)	-0.17 [-0.41, 0.08]	0.178
Sex (ref female)	-0.53 [-3.73, 2.67]	0.741
Spine levels fused	-0.36 [-1.10, 0.38]	0.332
Intrathecal morphine used (ref other)	0.47 [-4.75, 5.69]	0.857
Hospital morphine consumption (mg/kg/hr)	18.87 [-21.29, 59.03]	0.351
Hospital average pain score (NRS 0-10)	0.29 [-0.49, 1.06]	0.458
Baseline Widespread Pain (ref None)	-0.48 [-3.37, 2.40]	0.739
Symptom Cluster (ref Low Symptom Cluster)	9.92 [6.63, 13.2]	<0.001

NRS = Numeric Rating Scale

Legend for Figure:

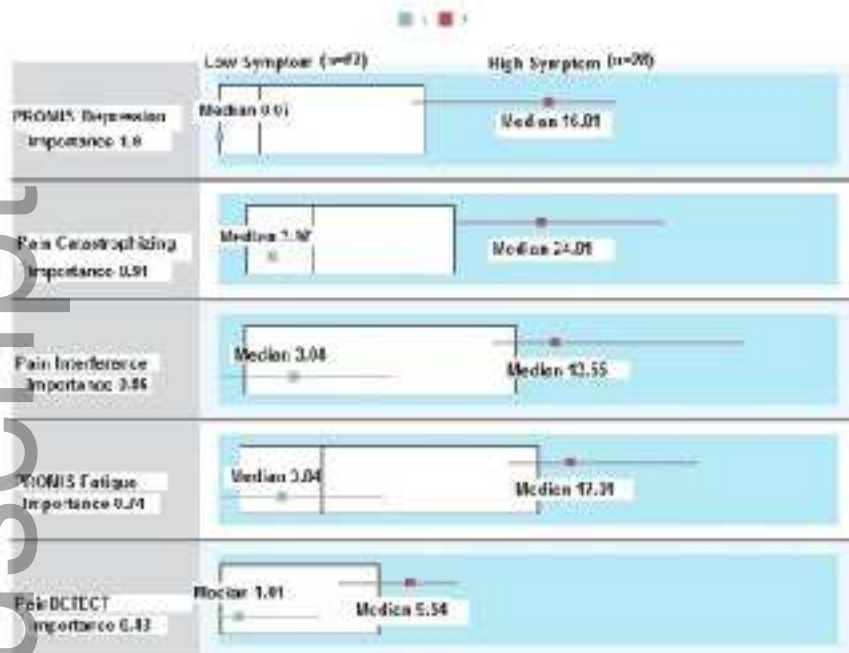
Figure 1. Description of Factors in Order of their Contribution to Low and High Symptom Cluster Membership. Results of the two-step cluster analysis; Silhouette measure of cohesion and separation >0.5 (good); Boxes depict the median (line) and 25th to 75th percentile range for the entire sample. The blue and red horizontal lines depict the interquartile range for the Low and High Symptom Cluster Groups respectively.

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Description of Clusters



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