Exploring interactions between sex, pain characteristics, disability, and quality of life in people with chronic spinal pain : a structural equation model

Exploring Interactions between Sex, Pain Characteristics, Disability, and Quality of Life in People with Chronic Spinal Pain: A Structural Equation Model

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Abstract

In people with nonspecific chronic spinal pain (nCSP), disability, and quality of life are associated with clinical, cognitive, psychophysical, and demographic variables. However, evidence regarding the interactions between these variables is only limited for this population. Therefore, this study aims to explore path models explaining the multivariate contributions of such variables to disability and quality of life in people with nCSP. This secondary analysis uses baseline data from a randomized controlled trial including 120 participants with nCSP. Structural equation modeling was used to explore path models for the Pain Disability Index (PDI), the Short Form 36-item physical (SF-36 PC), and mental (SF-36 MC) component scores. All models included sex, pain catastrophizing, kinesiophobia, hypervigilance, and pain intensity. Additionally, the PDI and SF-36 PC models included pressure pain thresholds at the dominant pain site (i.e., neck or low back). Significant associations were found between sex, pain cognitions, pain intensity, and pressure pain thresholds. Only pain catastrophizing significantly directly influenced the PDI ($p \leq 0.001$) and SF-36 MC ($p=0.014$), while the direct effects on the SF-36 PC from kinesiophobia ($p=0.008$) and pain intensity ($p=0.006$) were also significant. However, only the combined effect of all pain cognitions on the SF-36 PC was mediated by pain intensity ($p=0.019$). Our findings indicate that patients' pain-related cognitions have an adverse effect on their physical health-related quality of life via a negative influence on their pain intensity in people with nCSP.

Perspective

This secondary analysis details a network analysis confirming significant interactions between sex, pain cognitions, pain intensity, and pressure pain thresholds in relation to disability and health-related quality of life in people with chronic spinal pain. Moreover, its findings establish the importance of pain cognitions and pain intensity for these outcomes.

Keywords: Chronic spinal pain, kinesiophobia, pain catastrophizing, disability, health-related quality of life

Introduction

Nonspecific chronic spinal pain (nCSP), including neck and low back pain, is a prevalent worldwide condition affecting people of all ages.[9,28,30,45,49] Lifetime prevalence rates for spinal pain range from 54 to 80%, indicating that up to 80% of the general population experience an episode of spinal pain at least once in their lives.[45] nCSP is more common in women, and its prevalence increases with age, low educational status, higher body mass index, less physical activity, more psychological distress, and lower self-rated health.[4,26,45] Moreover, the socio-economic burden of nCSP is substantial and is considered one of the leading global causes of years lived with disability.[12,20,67]

Chronic pain conditions are known for complex interactions between various patient-related factors, which explain the heterogeneity in their clinical presentation.[11,19,27,41,64] For example, a recent study investigated the potential interactions between pain, psychological factors -including fear avoidance beliefs- and physical performance, and their relationship with disability in people with long-lasting low back pain.[41] Indeed, they found significant negative influences of pain and psychological factors on patients' disability, though the interactions with physical performance varied depending on symptom severity. An earlier study used cluster analyses to examine the associations between patients' demographic variables, diagnosis, and self-reported health status in people with spinal pain.[23] Their results indicate a significant role of gender, education level, and socio-economic factors in patients' self-reported functioning. However, no interaction between these factors was considered. Also, recent cluster analyses linked unfavorable scores of psychophysical measures, such as pain pressure thresholds and conditioned pain modulation, to increased pain intensity and disability in people with spinal pain.[10,15,54] Furthermore, one study described a maladaptive subgroup of people with low back pain who report lower pain modulation, as well as worse pain coping strategies.[10] Indeed, the findings of these studies indicate a complex interplay between different factors, such as pain intensity, psychophysical factors, and pain cognitions, in people with spinal pain. Moreover, symptoms of central sensitization, kinesiophobia, anxiety, psychophysical variables, and demographic characteristics were all found to be separately associated with disability or health-related quality of

life in people with nCSP, though so far, these influences were never investigated in interaction with each other.[18,37,43,50] Given the hypothesized interplay between these demographic, clinical and pain-related characteristics in people with nCSP, as well as the established associations between these characteristics and disability and health-related quality of life, a theoretical path model presents itself.[10,15,18,23,37,41,43,50,54] More specifically, based on the described evidence, a path model can be theorized linking the interactions between demographic, clinical, cognitive, and psychophysical aspects to explain the heterogeneity in functional status and health-related quality of life in people with nCSP. Indeed, such a model might help clarify why some people with nCSP report worse functional status and health-related quality of life than others, which, given the substantial individual burden of nCSP, will be valuable to develop targeted interventions.[12,20,67] However, so far, a path model combining interactions between demographic, clinical, cognitive, and psychophysical factors is lacking for people with nCSP.

Recently, causal mediation via structural equation modeling (SEM) is considered a valid approach to help disentangle mechanisms explaining the variability in clinical presentation in different conditions.[19,38,41,42] However, when utilizing cross-sectional data to build a path model, it is essential to first explore a theoretical framework based on the existing literature and clinical expertise to underline the assumed relationships in the proposed model.[62] Therefore, this study aims to explore and validate a path model using an SEM analysis explaining the multivariate contributions of demographic, clinical, cognitive, and psychophysical variables to health-related quality of life and functional status in people with nCSP.

Methods

Study design

This study is a secondary analysis using baseline data from a multicentered randomized controlled trial that assessed the effectiveness of Pain Neuroscience Education combined with cognition-targeted exercise therapy in people with nCSP. Data for the trial were collected from January

2014 to January 2016 in the University Hospitals of Ghent and Brussels, Belgium. The trial was prospectively registered at ClinicalTrials.gov (NCT02098005), and ethics approval was granted by the relevant ethics committees (i.e., University Hospital of Ghent, 2013/1133; University Hospital of Brussels, 2013/385). The full trial protocol has been published elsewhere.[21]

Participants

The original trial included 120 participants who fulfilled the following inclusion criteria: diagnosed with nCSP (i.e., neck or back pain for at least three days/week for at least three months), currently seeking care for low back or neck pain, native Dutch speaking, age 18 to 65 years, available and willing to participate in educational sessions, not starting new treatments or medication, and continuing usual care six weeks before and during study participation. People were excluded if they had specific medical conditions (i.e., neuropathic pain, neck or back surgery in prior three years, osteoporotic vertebral fractures, or rheumatologic diseases), a chronic widespread pain syndrome diagnosis, a place of residence more than 50 km (31 miles) away from the treatment location, contraindications related to magnetic resonance imaging, or if they were pregnant or gave birth in the year before the trial. Participants were recruited via the participating university hospitals, as well as occupational health services, primary care practices, social media, and advertisements. Written informed consent was obtained from all participants before their baseline assessment.

Observed variables

Outcomes

The Pain Disability Index (PDI) was used to assess participants' functional status and the degree to which pain interferes with their daily life.[61] The PDI evaluates family responsibilities, recreation, social activities, occupation, sexual behavior, self-care, and life support.

The Short-form 36-item Health Survey (SF-36) assessed participants' health-related quality of life.[1,71] The SF-36 includes questions regarding participants' physical functioning, role limitations due

to physical or emotional problems, bodily pain, vitality, social functioning, and mental health. The SF-36 physical and mental component scores were calculated and used in the analyses.

Predictors

Both pain intensity and central sensitization symptoms were evaluated as clinical measures. The Numeric Rating Scale for pain (NRS) evaluated pain intensity using an 11-point scale ranging from 0 ("no pain") to 10 ("worst pain imaginable").[25] Participants were asked to indicate their mean pain intensity at their neck or lower back during the last three days. Self-reported symptoms of central sensitization were assessed using the Central Sensitization Inventory (CSI).[47] This questionnaire comprises 25 statements regarding current health symptoms indicative of central sensitization and a checklist of previously diagnosed central sensitivity syndromes and related conditions.

Assessed pain cognitions include pain catastrophizing (i.e., having catastrophic thoughts and feelings regarding pain), kinesiophobia (i.e., fear of movement based on the (false) belief that movement might be harmful), and hypervigilance (i.e., having increased attention to, and awareness, consciousness, vigilance, and observation of pain), which were measured using the Pain Catastrophizing Scale (PCS), Tampa Scale for Kinesiophobia (TSK), and the Pain Vigilance and Awareness Questionnaire (PVAQ), respectively.[32,55-57,60,66] All used questionnaires are valid and reliable tools for chronic pain populations. [25,32,36,55-57,60,61,66]

The psychophysical variables include scores for the pressure pain thresholds (PPT) and conditioned pain modulation (CPM). Mechanosensitivity was assessed using pressure algometry to determine PPTs at symptomatic (i.e., upper trapezius muscle or 5cm lateral of L3 for people with neck or low back pain, respectively) and remote sites (i.e., quadriceps muscle and hand).[24,33,72] PPTs were taken unilaterally at the most painful side, or dominant side when the pain was evenly distributed. Values of people with neck pain and those with low back pain for the symptomatic (primary) test site were analyzed together. Additionally, the CPM paradigm was performed using PPT as the test stimuli, while a cold pressor test at the contralateral hand was added as the conditioning stimulus.[40,52] CPM was only evaluated at the primary testing site and the remote leg site. Participants were asked to rate

their pain intensity on an 11-point visual NRS. CPM scores were calculated as the absolute difference between the initial PPT and the PPT obtained during the cold pressor test. Both pressure algometry and CPM using the cold pressure test are widely used as clinical assessment tools for pain and are considered reliable measures.[40,52,68] A more detailed description of all included measures can be found in the published protocol.[21]

Approach to Structural Equation Modelling Analysis

Directed acyclic graph

A general directed acyclic graph (DAG) was developed to visualize the assumed relationships between the relevant predictors and outcome measures of interest (see **figure 1**). Interactions and their direction were chosen following a literature search and discussion between authors (WVB, BXWL, and AM).[18,23,37,43,50] The main relationships of interest are those between pain cognitions and disability and quality of life. As such, it is assumed that demographic characteristics directly influence patients' pain cognitions, clinical measures, and psychophysical factors but do not directly affect disability or quality of life in people with nCSP. Also, we consider pain cognitions to influence the self-reported scores for clinical measures and psychophysical factors at the time of assessment. Furthermore, psychophysical factors have an assumed direct effect on pain intensity, but not on disability or quality of life. Lastly, we assume that both clinical measures and cognitions directly influence disability and quality of life in people with nCSP. Overall, in the proposed DAG, only demographic characteristics are assumed exogenous variables, while clinical measures, pain cognitions, psychophysical factors, disability and quality of life are endogenous variables.

Correlation analysis

Associations between continuous predictors (i.e., demographic, clinical, cognitive, and psychophysical) and outcomes (i.e., disability and quality of life) were assessed using Pearson's correlation analyses and scatter plots. To account for all potentially significant associations, a cut-off of $p<0.10$ was used to identify those relevant for inclusion in the structural equation models.

Structural Equation Modelling (SEM)

SEM generates probabilistic models that unite multiple independent and dependent variables in a single model. Individual path models were created for the PDI, the SF-36 physical, and mental component scores. Based on the results of the correlation analyses (P-value < .10) and a literature search, only relevant predictors were included in each model. SEM analysis was used validate and fit these proposed path models (see figures 1 to 3.) Full Information Maximum Likelihood was used to estimate the model's parameters, while the 'Huber-White' robust standard errors were used. In all models, PCS, TSK and PVAQ were included in a parallel mediation structure, allowing for correlation among these pain cognitions (see figures 1 to 3.) To avoid overvaluing the importance of a single fit index, an excellent model fit is determined when two of the four fit indices exceed the thresholds: a root-mean-square error of approximation (RMSEA) ≤0.05; standard root mean residual (SRMR) ≤0.05; confirmatory fit index (CFI) ≥0.95; and non-normed fit index (NNFI) ≥0.95.[31] The 95% confidence interval (CI) of regression parameters was estimated using Montecarlo bootstrapping. For the estimated parameters, a P-value < .05 was considered to be statistically significant.

Packages

All analyses were performed in R Studio Version 1.4.1717 (R version 4.1.1, Boston, MA, USA).[53] The following packages were used: dagitty for DAG creation, mice for data imputation, lavaan for SEM analysis, semPlot for visualizing SEM paths, and semTools to fit an SEM across our 20 imputed datasets and to pool the statistical outputs using Rubin's rule.[22,34,58,63,65]

Results

Table 1 details the demographic and baseline characteristics of the participants. Results of the Pearson's correlation analyses evaluating the association between the continuous predictors and outcomes are shown in **Table 2**. The following predictors were included in the models for the PDI and the SF-36 physical component scores: participants' sex, dominant pain problem, and scores for the TSK, PCS, PVAQ, NRS, and PPT from the primary testing site. The model regarding the SF-36 mental

component scores only includes participants' sex, TSK, PCS, PVAQ, and NRS scores. Other demographic characteristics and the CPM scores were not included in any of the models, as they only had weak associations with the outcome measures. Due to the very strong correlations between the PPTs of the primary and secondary sites, we opted to only include one PPT measure in the models for PDI and SF-36 physical component scores. Given its relevance to the population, the PPT of the primary site was chosen.[44] As the testing site for this PPT measure was dependent on the dominant pain site, this relationship between these two factors was also included in the relevant models. The CSI was ultimately excluded from the SEM, as it has several statements that deal with psychological states (e.g., anxiety and depression) that are strongly associated with the cognitive factors included in the models.[37] Also, following factor analysis, its Dutch version -which was used in the original trial- was found to have an underlying factor 'General disability and physical symptoms,' which can partly explain the strong relationship between the CSI and the PDI, and SF-36.[36,37] However, an in-depth analysis including the different factors of the CSI falls outside the scope of this secondary analysis. Therefore, we only considered pain intensity, as assessed by the NRS, as a clinical factor in the models.

The path model for the PDI and its associated standardized regression weights (β) are reported in **Figure 2**. Additionally, the standard errors, 95% confidence intervals (CI), and P-values can be found in **Table 3**. The PDI model was shown to have an adequate fit (RMSEA = 0.07, CFI = 0.98, SRMR = 0.04, NNFI = 0.92). The R^2 (i.e., explained variance) for PDI was estimated to be 34.2%. Significant effects of PCS on PPT (β = -0.248; P = 0.026) and sex on PPT (β = -0.635; P = 0.001) were found. However, the effect of sex on PPT was not explained by any of the cognitive factors nor by their combined effect. Significant effects on the NRS were found for sex (β = 0.408; P = 0.012), PCS (β = 0.266; P = 0.015), and PVAQ (β = 0.264; P = 0.004), though these could not be explained via the PPT. Significant effects of PCS (β = 0.463; P = 0.000) and NRS (β = 0.172; P = 0.049) on the PDI were found. However, analyses showed no significant indirect effects via the NRS, indicating that the significant effect of PCS on PDI cannot be explained by NRS scores. No other significant direct effects on the PDI were found for any of the other predictors.

Table 4 and **Figure 3** show details regarding the path model for the SF-36 physical component scores. The fit measures for this model were adequate (RMSEA = 0.11, CFI = 0.95, SRMR = 0.05, NNFI = 0.80). The estimated R^2 for the SF-36 physical component score was 36.4%. As the path model is identical to the PDI model, the same significant effects were found for PPT~sex, PPT~PCS, NRS~sex, NRS~PCS, and NRS~PVAQ (see above). Additionally, significant direct effects of the TSK (β = -0.204; P = 0.008) and NRS (β = -0.255; P = 0.006) on the SF-36 physical component scores were found. However, the effect of the TSK could not be explained by the NRS. Though the indirect effect of the NRS on the relationship between the PCS and SF-36 physical component scores was not significant, the calculated 95%CI did not contain 0 (β = -0.069; P = 0.074). A similar result was found for the mediating effect of the NRS on the relationship between the PVAQ and SF-36 physical component scores (β = -0.067; P = 0.056). Regardless, the overall effect of cognitions on the SF-36 physical component was mediated via the effect of NRS (β = -0.131; P = 0.019). No other significant direct or indirect effects were found for the SF-36 physical component scores.

Finally, **Table 5** and **Figure 4** detail the path model for the SF-36 mental component scores. The model was shown to have a good fit (RMSEA = 0.00, CFI = 1.00, SRMR = 0.00, NNFI = 1.10). The R^2 for the mental component scores was estimated as 18.4%. For the NRS, significant direct effects of sex (β = 0.436; P = 0.007), PCS (β = 0.277; P = 0.013) and PVAQ (β = 0.259; P = 0.004) were found. Also, the analysis showed a significant direct effect of the PCS (β = -0.320; P = 0.014) on the SF-36 mental component scores. However, the NRS could not explain this effect of the PCS on the mental component scores. No other predictors had a significant direct or indirect effect on the SF-36 mental component scores.

Discussion

This study aimed to explore and validate path models explaining the multivariate contributions of demographic, clinical, cognitive, and psychophysical variables to health-related quality of life and functional status in people with nCSP. Though our analyses confirmed several

significant direct associations, only pain intensity was shown to mediate the combined effect of all pain cognitions on the SF-36 physical component score in these patients.

The main finding of this paper indicates that people with nCSP who have negative perceptions and beliefs about their pain will report a more intense pain experience, which in turn, will negatively impact their self-reported physical health-related quality of life. Also, the significant direct effects of kinesiophobia and pain catastrophizing on physical and mental health-related quality of life, respectively, indicate that patients' pain cognitions play an essential role in their health-related quality of life. Similarly, the significant direct influence of pain catastrophizing and hypervigilance on pain intensity confirms their relevance to patients' pain experience. Such relationships between pain cognitions and pain experience are well-established in people with chronic pain through the fear-avoidance model.[39,70] Moreover, in people with chronic low back pain, kinesiophobia and pain catastrophizing were found to be negatively associated with pain intensity, health-related quality of life, and disability.[2,5,13,35,59] However, evidence regarding the interrelationship between hypervigilance, pain intensity, and health-related quality of life is lacking in people with nCSP, underlining the importance of the current findings. Nevertheless, pain intensity was only found mediating the collective influence of pain cognitions, and not any of their individual effects. This might be explained by the underlying interactions between these cognitions, as they may strengthen each other's effect on patients' pain experience and, in turn, their health-related quality of life. Overall, our study showed the relevance of the negative relationship between pain cognitions and pain intensity for patients' health-related quality of life. More so, to the best of our knowledge, this is one of the first cross-sectional study to relate the association between pain cognitions and pain intensity with health-related quality of life in people suffering from nCSP. All these findings motivate further research to build upon the proposed path models and to thoroughly investigate the interactions among these pain cognitions when considering their relationship with pain intensity and health-related quality of life in this population.

296 Only pain catastrophizing was found to directly impact disability in people with nCSP. Given
297 that disability encompasses mainly physical aspects, the lack of a significant direct effect of
298 kinesiophobia is remarkable. However, this might be explained by the difference in activities described
299 in the used questionnaires. While the activities assessed in the PDI are all related to patients' daily life
300 (e.g., occupation, self-care), those discussed in the TSK reference physical activity or exercise.[32,57,61]
301 Consequently, the limitations that patients experience in their daily life activities may stem less from
302 their fear of movement (i.e., kinesiophobia) and more from other associated factors, such as how they
303 feel regarding their current pain (i.e., pain catastrophizing).

304 Next, our study showed significant direct effects of patients' sex on the primary PPTs and self-
305 reported pain intensity. Notably, female participants reported higher pain intensity and lower pain
306 thresholds at primary test sites than males, which is consistent with findings of earlier studies in other
307 populations.[8,14,29,46,48,51] Though it has been proposed that psychosocial factors might explain this sex
308 difference, our results indicate that patients' pain cognitions do not mediate the effect of sex on their
309 mechanosensitivity.[46] Nevertheless, our findings cannot exclude the possibility that interactions
310 between pain cognitions and biological factors (e.g., factors related to genetics, endocrine system, or
311 body composition) or other psychosocial factors influence the processing of mechanical stimuli. For
312 example, it would be possible that maladaptive cognitions combined with the hormonal fluctuations
313 during the menstrual cycle in female participants cause a change in pain thresholds, while such
314 interaction would be less relevant in male participants.[7,8,16] Additionally, based on our findings, we can
315 carefully assume that the influence of patients' sex on their pain intensity is not mediated by pain
316 cognitions or mechanosensitivity. Therefore, given the known influence of psychosocial factors (e.g.,
317 pain cognitions) on patients' pain experience, it might valuable to include gender, as a social construct,
318 in the interactions between sex and pain. [8,39,70] Nevertheless, further research is needed to identify
319 the pathways via which sex influences patients' mechanosensitivity and pain intensity, as well as their
320 interaction, in people with nCSP.

Currently, the multidimensional influence of demographic, cognitive, clinical, and psychophysical factors on disability and health-related quality of life in people with nCSP is not well-understood. As such, the current findings are relevant to the field. More specifically, the results of this SEM analysis motivate further research, wherein future models can be built based upon the currently presented models. Also, this study provides evidence supporting the inclusion of pain cognitions in such models regarding disability and health-related quality of life in people with nCSP. Moreover, although clinical implications are somewhat limited, our findings can motivate healthcare providers to consider patients' pain cognitions when treating people with nCSP who exhibit reduced functional status or poor health-related quality of life. Additionally, based on these findings, it can be stated healthcare providers should be aware that the impact of these patients' sex on their pain intensity is not mediated by any maladaptive pain cognitions, nor by any increased localized sensitivity, patients might have.

The SEM analysis reported a low degree of explained variance and a relatively small number of significant interactions, indicating that the proposed path models cannot fully explain the heterogeneity in functioning and health-related quality of life in people with nCSP. These restricted findings can be attributed to several limitations of this study. First, as our study is a secondary analysis of an original randomized controlled trial, we were limited in the number of included measures. It is possible that other factors, such as gender, physical activity, and socio-economic status, might play a significant role that we could not account for in these analyses. Therefore, future prospective studies should repeat these analyses in a similar, albeit larger, study sample and include more relevant predictors in the path model. Next, this secondary analysis comprised 120 participants, which may be considered limited for conducting a complex analysis like SEM. To address this potential limitation, Montecarlo bootstrapping was used to generate multiple resampled datasets, allowing us to more accurately calculate parameter estimates and their confidence intervals. Also, as we used baseline data of a randomized controlled trial that included participants already willing to follow an exercise intervention, our sample might not have included those patients with highly maladaptive cognitions

and beliefs regarding pain and movement (e.g., high kinesiophobia). This can impact the representativity of our results, as they might only be valid for those with a limited negative outlook on physical activity. Indeed, the mean TSK score of our study sample is 35.58 out of 68, which falls below the established cut-off indicating a maladaptive degree of kinesiophobia (37/68) and is substantially lower than those found in cross-sectional studies with similar study populations.[3,5,6,13,17,69] Lastly, our study was limited as a cross-sectional analysis, meaning that no conclusions regarding the causal relationship between variables could be made over time. However, by developing a DAG before the final analysis, we were able to infer certain directional relationships between the included variables at the time of assessment.[62]

Besides limitations, several strengths should also be discussed. First, our study sample comprises patients from several centers, with an equal distribution of people with neck (53%) and low back (47%) pain, allowing for a balanced study sample. Also, to deal with missing data, model parameters were estimated using a full information maximum likelihood method. Moreover, as only 5 participants did not complete all questionnaires, the impact of the missing data was limited. Next, by performing an SEM analysis, we were able to account for several variables in our models, which improved the validity of the associations found in our analysis. Also, this analysis allowed us to examine the established relationships between pain cognitions, pain intensity, and disability and health-related quality of life in interaction with other relevant factors (e.g., PPTs) in people with nCSP. Lastly, we were able to include a diverse set of pain-related measures (i.e., pain intensity, pain cognitions, PPTs, and dominant pain site), which allowed us to investigate the relationships between different subsets of pain characteristics in these patients.

Conclusions

Following an SEM analysis, significant associations were found between sex, PPTs, pain cognitions, and disability in people with nCSP, though the analyses showed no significant indirect effects between these variables. Similar results were found for the models related to health-related

quality of life. However, the total effect of all pain cognitions on the SF-36 physical component scores was mediated by pain intensity, indicating that patients' pain-related perceptions and beliefs have an adverse effect on their physical health via a negative influence on their pain experience. Nevertheless, to better understand the diversity in functional status and health-related quality of life, our findings motivate further exploration of the relationship between these outcomes and various pain characteristics.

Highlights

- Kinesiophobia directly impacts physical quality of life in people with chronic spinal pain
- Pain catastrophizing directly impacts patients' disability and mental quality of life
- Sex directly influences patients' pain intensity and pressure pain thresholds
- Pain intensity mediates the relationship between pain cognitions and physical quality of life

Disclosures

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Figure legends

Figure 1. The directed acyclic graph visualizing the assumed relationships between the demographic characteristics, pain cognitions, clinical measures, psychophysical factors, and outcome measures of interest (i.e., disability and quality of life) in people with chronic spinal pain.

Figure 2. The path model for the functional status scores (Pain Disability Index [PDI]), including participants' sex, dominant pain site (Site), and scores for the Tampa Scale for Kinesiophobia (TSK), Pain Catastrophizing Scale (PCS), Pain Vigilance and Awareness Questionnaire (PVAQ), Numeric Rating Scale for pain (NRS), and Pressure Pain Thresholds from the primary (symptomatic) testing site (i.e., at the level of the m. trapezius or the L3 vertebrae for people with neck or low back pain, respectively) with the associated standardized regression weights and significance levels of $p \leq .05$ (*); $p \leq .01$ (**); and $p \leq .001$ (***) (n=120). Correlation between the TSK, PCS, and PVAQ was considered by including them as parallel mediators in the model. However, these relationships are not presented in the path model for clarity reasons.

Figure 3. The path model for the physical health-related quality of life score (Short Form 36-item Health Survey physical component [SF-36 PC]), including participants' sex, dominant pain site (Site), and scores for the Tampa Scale for Kinesiophobia (TSK), Pain Catastrophizing Scale (PCS), Pain Vigilance and Awareness Questionnaire (PVAQ), Numeric Rating Scale for pain (NRS), and Pressure Pain Thresholds from the primary (symptomatic) testing site (i.e., at the level of the m. trapezius or the L3 vertebrae for people with neck or low back pain, respectively) with the associated standardized regression weights and significance levels of $p \leq .05$ (*); $p \leq .01$ (**); and $p \leq .001$ (***) (n=120). Correlation between the TSK, PCS, and PVAQ was considered by including them as parallel mediators in the model. However, these relationships are not presented in the path model for clarity reasons.

Figure 4. The path model for the mental health-related quality of life score (Short Form 36-item Health Survey mental component [SF-36 MC]), including participants' sex, and scores for the Tampa Scale for Kinesiophobia (TSK), Pain Catastrophizing Scale (PCS), Pain Vigilance and Awareness

Questionnaire (PVAQ), and Numeric Rating Scale for pain (NRS) with the associated standardized regression weights and significance levels of p≤.05 (*); p≤.01 (**); and p≤.001 (***) (n=120). Correlation between the TSK, PCS, and PVAQ was considered by including them as parallel mediators in the model. However, these relationships are not presented in the path model for clarity reasons.

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Tables

Table 1. Characteristics of participants with chronic spinal pain.

	Mean (SD)	Median (IQR) [Min; Max]	n
Age (yrs)	40.02 (12.54)	39.00 (23.00) [19; 65]	120
Pain duration (mts)	112.48 (92.31)	79.00 (132.00) [6; 420]	116
BMI	23.63 (3.58)	23.46 (4.66) [16.65; 36.11]	119
TSK (/68)	35.54 (7.04)	35.00 (9.25) [21; 61]	120
PCS (/52)	16.69 (10.11)	15.00 (15.00) [0; 48]	120
PVAQ (/80)	36.33 (12.26)	36.00 (17.25) [4; 70]	120
NRS (/10)	5.07 (1.89)	5.00 (3.00) [2; 10]	119
CSI (/100)	39.95 (11.36)	38.00 (14.00) [12; 72]	120
PPT (kgf)			
Primary site	4.47 (2.34)	4.00 (2.81) [0.13; 11.95]	115
Hand	3.60 (1.87)	3.23 (1.82) [0.12; 11.63]	115
Leg	5.20 (2.54)	4.81 (2.88) [0.30; 14.58]	115
CPM score			
Primary site	1.06 (1.34)	0.78 (1.49) [-1.77; 5.96]	108
Leg	0.96 (1.35)	0.75 (1.50) [-3.32; 7.31]	107
PDI (/70)	21.69 (13.97)	18.50 (18.00) [0; 63]	120
SF-36 PC (/400)	230.69 (73.76)	231.25 (113.75) [30.; 360]	120
SF-36 MC (/400)	279.79 (70.35)	289.00 (89.96) [85; 390]	120
		n (%)	
Dominant pain problem			
Neck pain		64 (53.33)	
Low back pain		56 (46.67)	
Sex			
Male		47 (39.17)	
Female		73 (60.83)	
Education level			
Lower secondary school		12 (10.00)	
Higher secondary school		24 (20.00)	
Higher education		84 (70.00)	

BMI= Body Mass Index, calculated as weight in kilograms divided by height in meters squared; CPM= Conditioned Pain Modulation, calculated as the absolute difference between the initial pain pressure threshold and the pain pressure threshold during a cold pressure test; CSI= Central Sensitization Inventory; IQR= Interquartile range; kgf= kilogram-force; MC = Mental component; mts= months; n= Number of participants; PC= Physical component; PCS= Pain Catastrophizing Scale; PDI= Pain Disability Index; PPT= Pressure Pain Threshold; prim.= primary (symptomatic) site for quantitative sensory testing (i.e., upper trapezius muscle or 5 cm lateral of L3); PVAQ= Pain Vigilance and Awareness Questionnaire; SD= Standard deviation; SF-36= Short Form 36-item Health Survey; TSK= Tampa Scale for Kinesiophobia; yrs= years.

Table 2. Results of the Pearson's correlation analyses evaluating the association between the outcome measures of interest of participants with chronic spinal pain.

	Age	BMI	Pain duration	NRS	CSI	TSK	PCS	PVAQ	PPT prim.	PPT sec.	CPM prim.	CPM sec.	PDI	SF-36 PC	SF-36 MC
Age	1														
BMI	0.30***	1													
Pain duration	0.22*	0.10	1												
NRS	-0.03	-0.01	-0.15	1											
CSI	-0.10	-0.06	-0.03	0.35***	1										
TSK	0.01	0.11	-0.03	0.16†	0.25**	1									
PCS	-0.06	-0.004	-0.18†	0.43***	0.46***	0.44***	1								
PVAQ	0.03	-0.05	-0.05	0.42***	0.25**	0.30***	0.65***	1							
PPT prim.	0.25**	0.18*	0.12	-0.16†	-0.21*	-0.03	-0.13	-0.01	1						
PPT sec.	0.26**	0.21*	0.02	-0.18†	-0.29**	0.02	-0.15	-0.07	0.81***	1					
CPM prim.	0.03	0.02	-0.13	-0.004	-0.05	0.03	0.04	-0.02	0.32***	0.41***	1				
CPM sec.	-0.07	-0.04	0.01	-0.15	0.02	-0.07	0.06	-0.02	0.09	0.04	0.49***	1			
PDI	0.05	0.02	-0.16†	0.37***	0.48***	0.30***	0.56***	0.38***	-0.16†	-0.13	0.14	0.13	1		
SF-36 PC	-0.09	-0.07	0.10	-0.44***	-0.62***	-0.38***	-0.50***	-0.47***	0.21*	0.22*	0.01	-0.01	-0.78***	1	
SF-36 MC	0.07	0.08	0.03	-0.31***	-0.64***	-0.19*	-0.40***	-0.28**	0.08	0.13	0.05	-0.04	-0.37***	0.45***	1

BMI= Body Mass Index; CPM= Conditioned Pain Modulation, the effect is calculated as the relative difference between the Numeric Rating Scale scores of the first and second part of the CPM-paradigm; CSI= Central Sensitization Inventory; MC = Mental Component; NRS= Numeric Rating Scale for pain; Pain duration= number of months participants reported having complaints; PC= Physical Component; PCS= Pain Catastrophizing Scale; PDI= Pain Disability Index; PPT= Pressure Pain Threshold; prim.= primary (symptomatic) site for quantitative sensory testing (i.e., upper trapezius muscle or 5 cm lateral of L3); PVAQ= Pain Vigilance and Awareness Questionnaire; sec.= secondary (asymptomatic) site for quantitative sensory testing, calculated as the mean score of remote sites (i.e., quadriceps muscle and hand); SF-36= Short Form 36-item Health Survey; TSK= Tampa Scale for Kinesiophobia (†:p≤0.1; *:p≤.05; **:p≤.01;***:p≤.001).

Table 3. Results of the structural equation modelling showing the standardized parameter estimates for the model regarding the Pain Disability Index in participants with chronic spinal pain (n= 120).

Dependent variables	Independent variables	β	SE	z-value	95% CI	P-value	Sig.
TSK	Sex	-0.172	0.181	-0.946	-0.525 to 0.185	0.344	ns
PCS	Sex	-0.161	0.195	-0.826	-0.537 to 0.223	0.409	ns
PVAQ	Sex	-0.155	0.190	-0.817	-0.529 to 0.214	0.414	ns
PPT	Sex	-0.635	0.195	-3.256	-1.020 to -0.248	0.001	s
PPT	TSK	0.011	0.095	0.117	-0.173 to 0.192	0.907	ns
PPT	PCS	-0.248	0.111	-2.233	-0.463 to -0.029	0.026	s
PPT	PVAQ	0.127	0.116	1.101	-0.099 to 0.355	0.271	ns
PPT	Dominant pain site	0.124	0.176	0.701	-0.225 to 0.468	0.483	ns
NRS	Sex	0.408	0.163	2.504	0.083 to 0.728	0.012	s
NRS	TSK	-0.018	0.086	-0.206	-0.184 to 0.145	0.837	ns
NRS	PCS	0.266	0.109	2.433	0.052 to 0.481	0.015	s
NRS	PVAQ	0.264	0.091	2.918	0.087 to 0.441	0.004	s
NRS	PPT	-0.045	0.075	-0.598	-0.189 to 0.102	0.550	ns
PDI	TSK	0.079	0.072	1.092	-0.063 to 0.221	0.275	ns
PDI	PCS	0.463	0.102	4.526	0.264 to 0.663	0.000	s
PDI	PVAQ	-0.015	0.089	-0.167	-0.190 to 0.161	0.868	ns
PDI	NRS	0.172	0.087	1.969	0.001 to 0.343	0.049	s
PPT†	TSK*Sex	-0.002	0.017	-0.115	-0.058 to 0.045	0.908	ns
PPT†	PCS*Sex	0.040	0.050	0.795	-0.062 to 0.161	0.426	ns
PPT†	PVAQ*Sex	-0.020	0.029	-0.681	-0.106 to 0.043	0.496	ns
PPT†	Cognitions*Sex	0.018	0.038	0.480	-0.076 to 0.113	0.631	ns
NRS†	TSK*PPT	0.000	0.004	-0.118	-0.017 to 0.019	0.906	ns
NRS†	PCS*PPT	0.011	0.018	0.604	-0.031 to 0.053	0.546	ns
NRS†	PVAQ*PPT	-0.006	0.011	-0.535	-0.038 to 0.019	0.592	ns
NRS†	Cognitions*PPT	0.005	0.009	0.542	-0.015 to 0.032	0.588	ns
PDI†	TSK*PPT*NRS	0.000	0.001	-0.117	-0.003 to 0.004	0.907	ns
PDI†	TSK*NRS	-0.003	0.015	-0.205	-0.039 to 0.029	0.838	ns
PDI†	TSK*PPT*NRS + TSK*NRS	-0.003	0.015	-0.210	-0.039 to 0.030	0.833	ns
PDI†	PCS*PPT*NRS	0.002	0.003	0.548	-0.005 to 0.013	0.583	ns
PDI†	PCS*NRS	0.046	0.031	1.452	-0.001 to 0.124	0.146	ns
PDI†	PCS*PPT*NRS + PCS*NRS	0.048	0.033	1.443	-0.001 to 0.130	0.149	ns
PDI†	PVAQ*PPT*NRS	-0.001	0.002	-0.499	-0.008 to 0.003	0.617	ns
PDI†	PVAQ*NRS	0.045	0.028	1.599	0.000 to 0.113	0.110	ns
PDI†	PVAQ*PPT*NRS + PVAQ*NRS	0.044	0.028	1.598	0.000 to 0.111	0.110	ns
PDI†	Cognitions*PPT*NRS + Cognitions*NRS	0.089	0.051	1.759	0.000 to 0.200	0.079	ns
NRS†	TSK*PPT*Sex	0.000	0.001	0.116	-0.005 to 0.005	0.908	ns
NRS†	PCS*PPT*Sex	-0.002	0.004	-0.485	-0.015 to 0.008	0.627	ns
NRS†	PVAQ*PPT*Sex	0.001	0.002	0.462	-0.005 to 0.009	0.644	ns
NRS†	PPT*Sex	0.028	0.049	0.577	-0.064 to 0.144	0.564	ns
NRS†	Cognitions*PPT*Sex	0.028	0.048	0.577	-0.062 to 0.140	0.564	ns

95% CI= Montecarlo Bootstrapped 95% Confidence Interval; β= standardized regression weights; Cognitions= Combined effects of the TSK, PCS, and PVAQ; Dominant pain site= Patients reported their dominant pain problem (i.e., neck pain or low back pain); NRS= Numeric Rating Scale for pain; PCS= Pain Catastrophizing Scale; PDI= Pain Disability Index; PPT= Pressure Pain Threshold from the primary (symptomatic) testing site (i.e., upper trapezius muscle or 5 cm lateral of L3); PVAQ= Pain Vigilance and Awareness Questionnaire; SE= Standard error; Sig.= significance level (i.e., s= significant; ns= not significant); TSK= Tampa Scale for Kinesiophobia.

† Indirect effects

Table 4. Results of the structural equation modelling showing the standardized parameter estimates for the model regarding the physical component scores of the Short Form 36-item Health Survey in participants with chronic spinal pain (n= 120).

Dependent variables	Independent variables	β	SE	z-value	95% CI	P-value	Sig.
TSK	Sex	-0.172	0.181	-0.946	-0.529 to 0.178	0.344	ns
PCS	Sex	-0.161	0.195	-0.826	-0.542 to 0.221	0.409	ns
PVAQ	Sex	-0.155	0.190	-0.817	-0.531 to 0.221	0.414	ns
PPT	Sex	-0.635	0.195	-3.257	-1.017 to -0.256	0.001	s
PPT	TSK	0.011	0.095	0.118	-0.175 to 0.200	0.906	ns
PPT	PCS	-0.248	0.111	-2.229	-0.465 to -0.030	0.026	s
PPT	PVAQ	0.127	0.116	1.100	-0.098 to 0.353	0.271	ns
PPT	Dominant pain site	0.123	0.177	0.698	-0.227 to 0.467	0.485	ns
NRS	Sex	0.415	0.164	2.533	0.092 to 0.733	0.011	s
NRS	TSK	-0.018	0.086	-0.205	-0.183 to 0.150	0.838	ns
NRS	PCS	0.261	0.110	2.384	0.044 to 0.475	0.017	s
NRS	PVAQ	0.267	0.091	2.939	0.091 to 0.446	0.003	s
NRS	PPT	-0.045	0.075	-0.594	-0.190 to 0.101	0.553	ns
SF-36 PC	TSK	-0.204	0.078	-2.634	-0.354 to -0.051	0.008	s
SF-36 PC	PCS	-0.182	0.108	-1.679	-0.401 to 0.034	0.093	ns
SF-36 PC	PVAQ	-0.181	0.097	-1.863	-0.374 to 0.010	0.063	ns
SF-36 PC	NRS	-0.255	0.093	-2.735	-0.439 to -0.072	0.006	s
PPT†	TSK*Sex	-0.002	0.017	-0.116	-0.060 to 0.045	0.908	ns
PPT†	PCS*Sex	0.040	0.050	0.795	-0.063 to 0.159	0.427	ns
PPT†	PVAQ*Sex	-0.020	0.029	-0.680	-0.107 to 0.045	0.496	ns
PPT†	Cognitions*Sex	0.018	0.038	0.480	-0.076 to 0.113	0.631	ns
NRS†	TSK*PPT	0.000	0.004	-0.118	-0.017 to 0.019	0.906	ns
NRS†	PCS*PPT	0.011	0.018	0.600	-0.032 to 0.053	0.548	ns
NRS†	PVAQ*PPT	-0.006	0.011	-0.533	-0.038 to 0.019	0.594	ns
NRS†	Cognitions*PPT	0.005	0.009	0.539	-0.015 to 0.033	0.590	ns
SF-36 PC†	TSK*PPT*NRS	0.000	0.001	0.118	-0.005 to 0.005	0.906	ns
SF-36 PC†	TSK*NRS	0.004	0.022	0.205	-0.044 to 0.052	0.838	ns
SF-36 PC†	TSK*PPT*NRS + TSK*NRS	0.005	0.022	0.210	-0.044 to 0.052	0.834	ns
SF-36 PC†	PCS*PPT*NRS	-0.003	0.005	-0.564	-0.017 to 0.008	0.573	ns
SF-36 PC†	PCS*NRS	-0.067	0.037	-1.801	-0.152 to -0.006	0.072	ns
SF-36 PC†	PCS*PPT*NRS + PCS*NRS	-0.069	0.039	-1.789	-0.159 to -0.006	0.074	ns
SF-36 PC†	PVAQ*PPT*NRS	0.001	0.003	0.509	-0.005 to 0.012	0.611	ns
SF-36 PC†	PVAQ*NRS	-0.068	0.036	-1.913	-0.155 to -0.011	0.056	ns
SF-36 PC†	PVAQ*PPT*NRS + PVAQ*NRS	-0.067	0.035	-1.908	-0.152 to -0.010	0.056	ns
SF-36 PC†	Cognitions*PPT*NRS + Cognitions*NRS	-0.131	0.056	-2.345	-0.256 to -0.033	0.019	s
NRS†	TSK*PPT*Sex	0.000	0.001	0.116	-0.005 to 0.005	0.907	ns
NRS†	PCS*PPT*Sex	-0.002	0.004	-0.484	-0.014 to 0.008	0.628	ns
NRS†	PVAQ*PPT*Sex	0.001	0.002	0.461	-0.005 to 0.009	0.645	ns
NRS†	PPT*Sex	0.028	0.049	0.573	-0.063 to 0.144	0.567	ns
NRS†	Cognitions*PPT*Sex	0.028	0.048	0.573	-0.062 to 0.141	0.567	ns

95% CI= Montecarlo Bootstrapped 95% Confidence Interval; β= standardized regression weights; Cognitions= Combined effects of the TSK, PCS, and PVAQ; Dominant pain site= Patients reported their dominant pain problem (i.e., neck pain or low back pain); NRS= Numeric Rating Scale for pain; PCS= Pain Catastrophizing Scale; PPT= Pressure Pain Threshold from the primary (symptomatic) testing site (i.e., upper trapezius muscle or 5 cm lateral of L3); PVAQ= Pain Vigilance and Awareness Questionnaire; SE= Standard error; SF-36 PC = Physical component scores of the Short Form 36-item Health Survey; Sig.= significance level (i.e., s= significant; ns= not significant); TSK= Tampa Scale for Kinesiophobia.

† Indirect effects

Table 5. Results of the structural equation modelling showing the standardized parameter estimates for the model regarding the mental component scores of the Short Form 36-item Health Survey in participants with chronic spinal pain (n= 120).

Dependent variables	Independent variables	β	SE	z-value	95% CI	P-value	Sig.
TSK	Sex	-0.172	0.181	-0.946	-0.532 to 0.184	0.344	ns
PCS	Sex	-0.161	0.195	-0.826	-0.542 to 0.220	0.409	ns
PVAQ	Sex	-0.155	0.190	-0.817	-0.529 to 0.214	0.414	ns
NRS	Sex	0.436	0.162	2.696	0.123 to 0.750	0.007	s
NRS	TSK	-0.019	0.086	-0.217	-0.188 to 0.152	0.828	ns
NRS	PCS	0.277	0.112	2.476	0.061 to 0.494	0.013	s
NRS	PVAQ	0.259	0.091	2.851	0.082 to 0.436	0.004	s
SF-36 MC	TSK	-0.020	0.084	-0.235	-0.184 to 0.144	0.814	ns
SF-36 MC	PCS	-0.320	0.130	-2.470	-0.575 to -0.068	0.014	s
SF-36 MC	PVAQ	0.000	0.107	-0.003	-0.210 to 0.210	0.998	ns
SF-36 MC	NRS	-0.169	0.090	-1.883	-0.345 to 0.004	0.060	ns
SF-36 MC†	TSK*NRS	0.003	0.014	0.221	-0.036 to 0.034	0.825	ns
SF-36 MC†	PCS*NRS	-0.047	0.030	-1.536	-0.120 to 0.003	0.125	ns
SF-36 MC†	PVAQ*NRS	-0.044	0.028	-1.580	-0.109 to 0.002	0.114	ns
SF-36 MC†	Cognitions*NRS	-0.087	0.051	-1.726	-0.199 to 0.002	0.084	ns

95% CI= Montecarlo Bootstrapped 95% Confidence Interval; β= standardized regression weights; Cognitions= Combined effects of the TSK, PCS, and PVAQ; NRS= Numeric Rating Scale for pain; PCS= Pain Catastrophizing Scale; PVAQ= Pain Vigilance and Awareness Questionnaire; SE= Standard error; SF-36 MC = Mental component scores of the Short Form 36-item Health Survey; Sig.= significance level (i.e., s= significant; ns= not significant); TSK= Tampa Scale for Kinesiophobia.

† Indirect effects

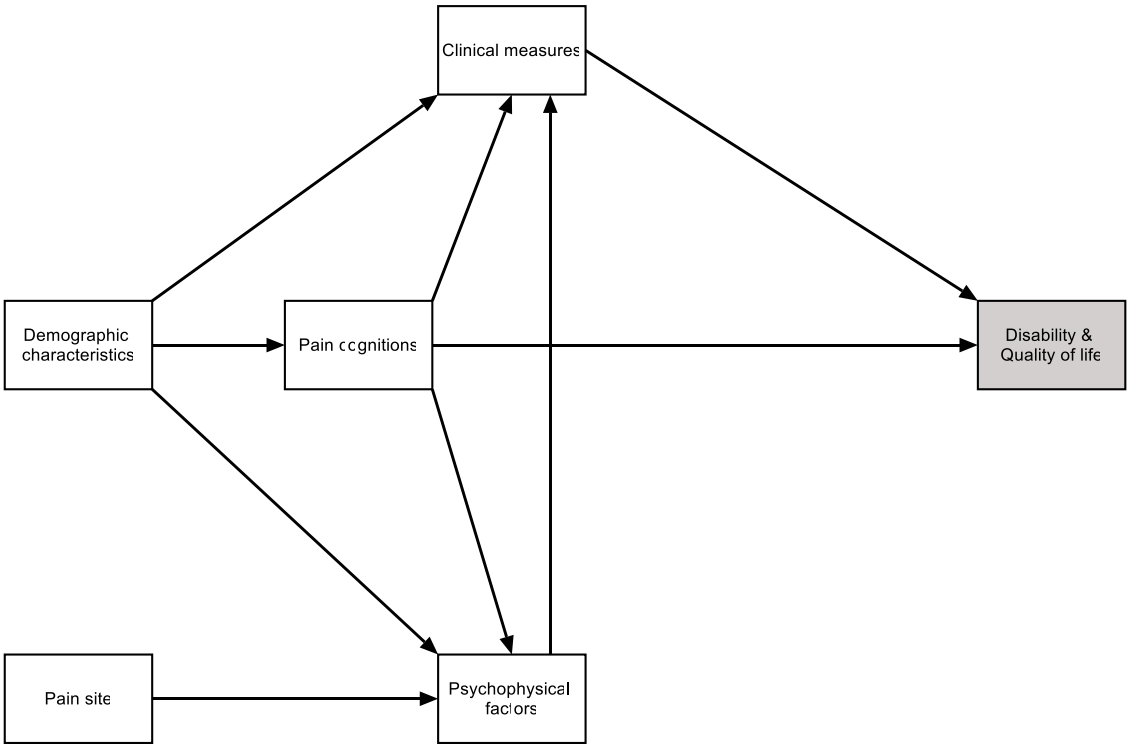

Figure 1.

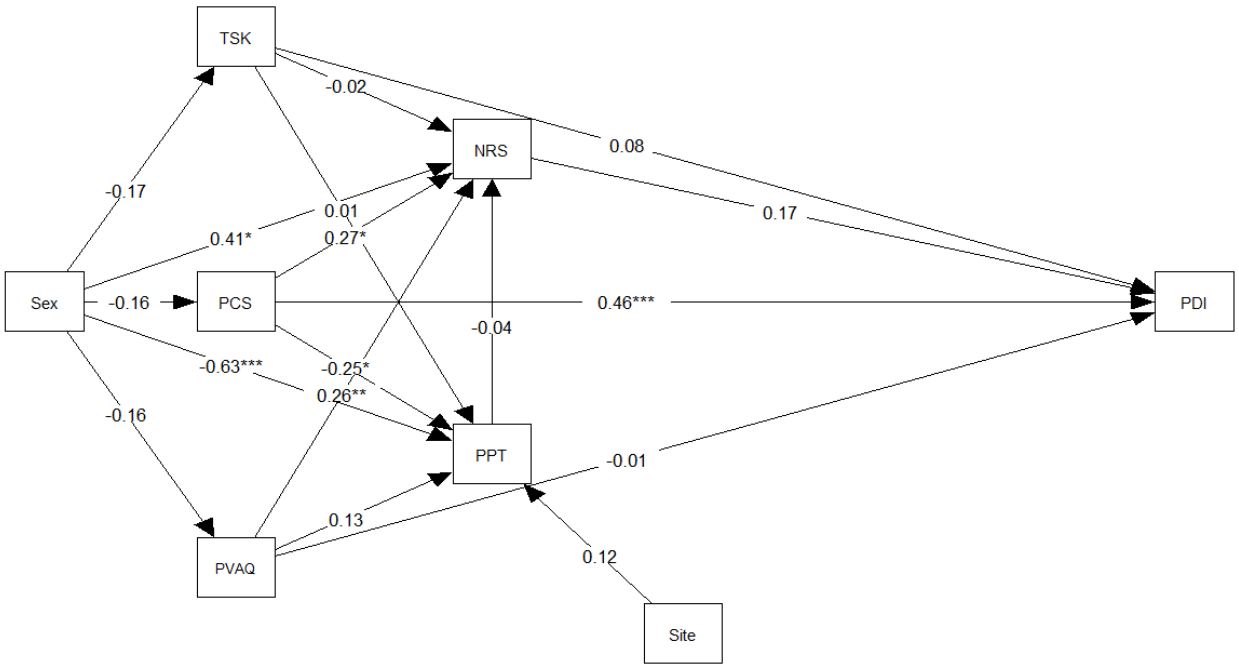

Figure 2.

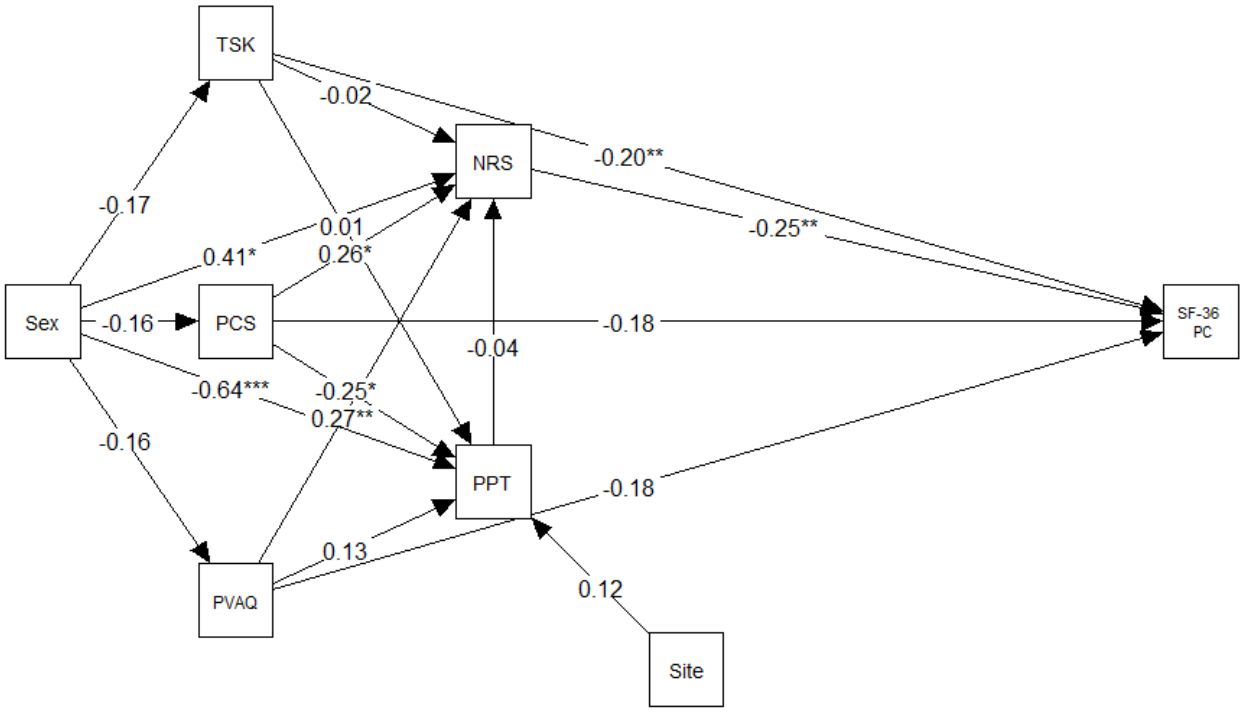

Figure 3.

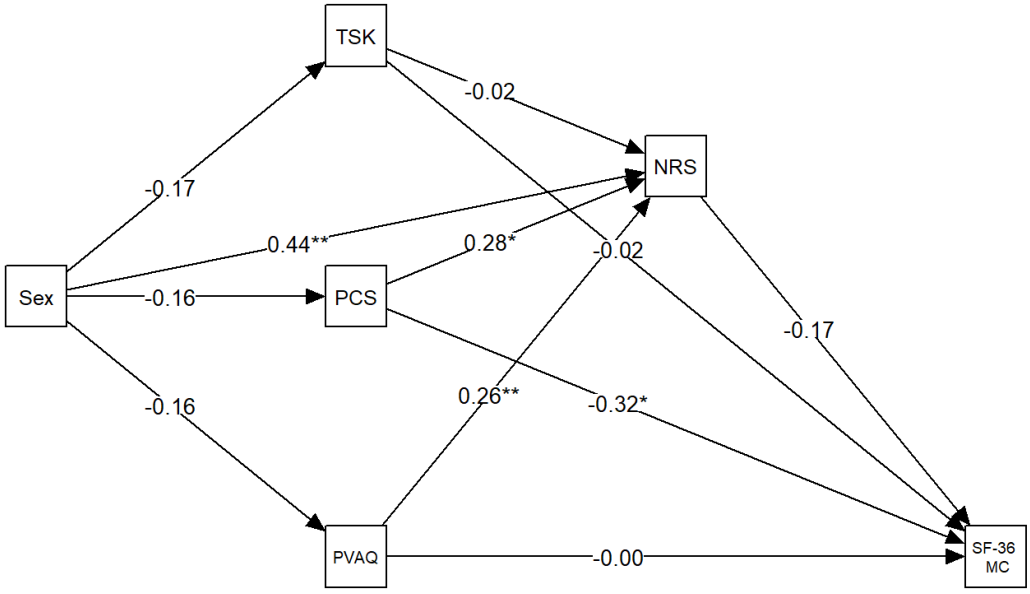

Figure 4.