

Clinical Pain Research

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Different pain variables could independently predict anxiety and depression in subjects with chronic musculoskeletal pain

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Abstract

Objectives: Chronic, clinical pain states are often accompanied by distress such as anxiety and depression. The aim of this study was to determine if certain clinical pain variables could predict the level of anxiety and depression in subjects with musculoskeletal pain.

Methods: Two multiple linear regression analyses were conducted on a sample consisting of 189 subjects with clinical pain with the independent pain variables of pain intensity, the influence of pain on daily activities, pain persistence, pain duration, and the number of pain locations. The dependent variables measured anxiety and depression, respectively.

Result: Two statistically significant models were found, where the predicted variables accounted for 37.0% of the variability in the anxiety levels and 43.7% of the variability in the depression levels. The independent variable, the influence of pain on daily activities, significantly predicted the level of anxiety. The variables, the influence of pain on daily activities and the number of pain locations, significantly predicted the levels of anxiety and depression.

Conclusions: This study showed that two different independent variables, the influence of pain on daily activities and the number of pain locations, significantly predicted the levels of depression. The predictor, the influence of pain on daily activities, significantly predicted the levels of

anxiety. The knowledge gained about which specific pain variables are more likely to coexist with anxiety and depression in clinical pain states could be important in implementing holistic treatment plans for chronic pain.

Keywords: anxiety; chronic pain; clinical musculoskeletal pain; depression; multiple linear regression analyses; pain qualities.

Introduction

Approximately 19% of adult Europeans suffer from moderate to severe chronic pain according to the Pain in Europe survey [1]. It is well-known that chronic pain states are accompanied by anxiety, depression, disturbed sleep, and fear [2–7]. Feelings of frustration, guilt, confusion, anger and a fear of never knowing about how intense the pain will be in the near or distant future have been reported from individuals with chronic pain [8]. Anxiety and depression tend to increase pain intensity and suffering in individuals with chronic pain and individuals with high levels of anxiety and depression are at risk for utilising health care resources to a high degree [9–11]. Furthermore, anxiety is often a precursor of depression, and consequently, it is important to detect anxiety in individuals with chronic pain states [4].

The activation of the insular cortex and the anterior cingulate cortex in pain states has been suggested to be responsible for the affective-emotional component of pain [12] and structural alterations in the insular cortex have been shown in major depression [13]. Following this, pre-existing anxiety or depression was found to be related to musculoskeletal pain in health-care workers and it has been shown that depression and pain severity seem to have a reciprocal relationship since increased depression predicted increased pain severity but increased pain severity also predicted increased depression [14, 15]. Higher pain intensity ratings and pain in more locations also correlated with higher ratings of anxiety and depression in a longitudinal design [16]. It has been concluded that 39% of the

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subjects in a chronic pain sample suffered from anxiety disorder and 31% of the individuals suffered from depression [17]. Yet another study examined the relationship between anxiety and depression in individuals with chronic neck pain and found that different pain variables, such as experienced disability and radiating pain in the upper extremities were independently associated with both anxiety and depression [18].

The data in this study were also analysed in three previous studies, where anxiety and depression levels were measured as control variables in the analyses of cognitive function in subjects with musculoskeletal pain [19–21]. In these analyses, pain, anxiety and depression levels were strongly correlated. From daily clinical practice with patients suffering from musculoskeletal pain, the question arose about which pain variables are the most closely correlated with the levels of anxiety and depression.

Examining the predictive abilities of different pain variables could be clinically important even if a causal relationship could not be established. Chronic pain treatment must intervene with factors that aggravate the pain condition since it is not possible to cure chronic pain. If we know which specific pain variables have the greatest influence on the feeling of anxiety and/or depression it may be possible to treat these variables more specifically in order to reduce the psychological impact.

The aim of this study was to determine if different clinical pain variables could predict the level of anxiety and depression in subjects with chronic musculoskeletal pain.

Materials and methods

Study design and setting

In this study, a cross-sectional study design was used and the data were collected in three earlier studies examining the relationship between clinical pain and cognitive abilities [19–21] (referred to as Studies 1, 2 and 3, respectively). The subjects were separately recruited to each of the earlier studies [19–21]. They were recruited when seeking a physiotherapist for treatment of musculoskeletal pain at a primary care centre in southern Sweden in two periods, first from January 2017 – October 2017 (Study 1), and from October 2018 – June 2019 (Study 2). Information about Study 2 and 3 were published on the Swedish Fibromyalgia Syndrome Union's website (which is a patient support group) and subjects were recruited to participate in the studies from this website between April 2019 and October 2019. Subjects were also recruited to Study 3 via information pamphlets about the study in waiting rooms at primary care centres in the southeast of Sweden between September and November 2019. That means that in study 2 and 3, subjects from both the patient union and from the primary care centre participated. The patients recruited from the patient union's

website were living in different areas in Sweden. None of the subjects from the patient union participated in both Study 2 and 3. In Study 1, 116 subjects were assessed for eligibility, but 7 subjects declined to participate. In Study 2, 183 subjects were assessed for eligibility (70 from the patient union, and 113 from the primary care centre), but 74 subjects declined to participate. In Study 3, 127 subjects were assessed for eligibility (109 from the patient union and 18 from the primary care centre) but 31 subjects declined to participate. This left 109 subjects from Study 1, 109 subjects from Study 2 and 96 subjects from Study 3 and the data matrixes from these three studies were put together into one data matrix containing a total of 314 subjects. All subjects with incomplete answers in any of the current predictors or outcome variables ($n=52$) or participating in both study 1 and 2 ($n=6$) were excluded ($n=58$). From the 58 excluded subjects, 7 were from Study 1, 44 from Study 2 and 7 from Study 3. In the end 256 subjects were included. After this, all subjects with a pain duration shorter than 90 days were excluded from the study (67 subjects in total; 39 from Study 1, 23 from Study 2, and 5 from Study 3) and after this exclusion 189 subjects remained (83 subjects with a fibromyalgia diagnosis and 106 subjects with other musculoskeletal diagnoses) (see Figure 1 and Table 1).

Inclusion criteria were subjects with perceived pain from muscles and/or joints and Swedish language fluency. Exclusion criteria were age below 18 years. Subjects with chronic musculoskeletal pain were chosen since musculoskeletal pain states are common in Western societies and are responsible for high societal costs [1, 22, 23].

Study 1 and 2 were approved in the same ethical application by the regional ethics review board in Linköping (code 2015/432-31) and

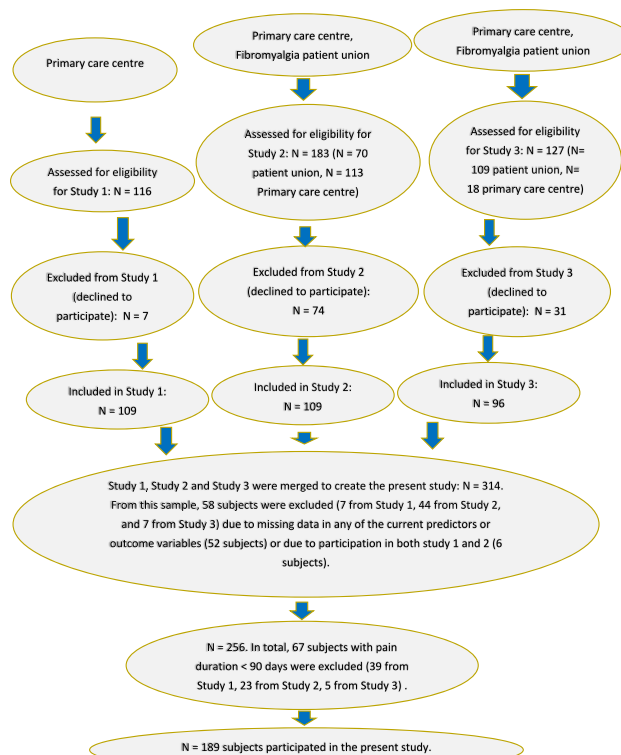


Figure 1: Flow diagram describing the recruitment procedure for the earlier studies and the present study. Flow diagram depicting the flows of the study subjects from the three original cohorts from study 1, 2 and 3 (Ref. [19–21]) to the present study.

Table 1: Number of participants in the different pain diagnoses according to ICD-10.

	Fibromyalgia syndrome (M797)	Other (M545), (M542), (M544), (M754), (M706), (M17), (M771), (S46), (M755), (M81), (M654), (S834), (S836), (G58), (M19), (G540), (M255), (M16), (M79).
Number of participants	81	108

Study 3 was approved by the ethics review board in Linköping code (code: 2019-02071). A new application to the regional ethics board in Linköping was approved for the present study since we performed different analyses of the data material and had new framings of questions (code: 2019-06515).

Regarding the subjects seeking a physiotherapist for musculoskeletal pain treatment, the physiotherapist examined and diagnosed each subject and wrote the diagnosis in the questionnaire. The subjects marked the painful areas on a human figure in the Brief Pain Inventory-Short Form (BPI-SF) and the marked areas matched the diagnosis in all participating individuals in this group. The subjects recruited from the patient union had received their fibromyalgia diagnosis from a doctor and they reported their diagnosis in the questionnaire and in the BPI-SF where they marked the areas where they felt pain on a human figure. The marked areas matched the diagnosis in all but five cases with a fibromyalgia diagnosis. In these five pain drawings, there was pain in less than four body regions (3 body regions) despite the fibromyalgia diagnosis.

Procedure

The data were collected in three earlier studies examining the relationship between clinical pain and cognitive abilities. The information published on the patient union website contained contact information for the study director (HG). Those wanting to participate emailed the study director for further information and following that information all of those interested provided a physical address for the questionnaire to be sent to. The questionnaire was sent to the subjects with instructions to answer the questions alone in a peaceful and quiet environment. After answering the questionnaire, the subjects sent it back to the study director in a freepost envelope. The subjects recruited at the primary care centre in Study 1 and 2 when seeking a physiotherapist for musculoskeletal pain treatment filled in the form in a quiet room at the primary care centre and handed it back to the physiotherapist who delivered it to the study director (HG).

The independent variables

The following 6 independent variables were included in this study since it was hypothesised that some variables in the pain experience would predict anxiety and depression, independently of and to different extents than others.

Reported pain intensity and influence on daily activities: To measure the present pain intensity at the test session, the subjects estimated their perceived pain on a visual analogue scale (VAS). On a 10 cm

horizontal line, the subject placed a mark between the two endpoints: no pain and worst pain imaginable. The subjects received a score based on the distance on the 10 cm line between the 'no pain' and 'worst pain imaginable'. The VAS is a subjective scale, since every pain experience is subjective, which means that other factors external to the immediate pain sensation, such as current mood, past experiences, and expectations, could influence every pain rating [24]. In spite of this, the VAS is a traditional method of pain measurement and the scale has several benefits; it is simple, effective, and widely used in both research and clinical practice [25]. Moreover, the VAS has been reported to be a valid scale when measuring experimental and chronic pain [26]. Cut-off points on VAS for pain-intensity-related interference with functioning have been suggested with mild (<3.4), moderate (3.5–6.4), and severe pain-related interference (>6.5) [27]. The subjects were asked to estimate their pain intensity and the influence of their pain on daily activities during the last 24 h in the BPI-SF. The BPI-SF has been widely used in different countries, and good reliability and validity have been reported [28]. The scale in the BPI-SF ranged from 0 (no pain) to 10 (worst pain imaginable) for BPI-SF-intensity, and from 0 (no influence) and 10 (very large influence) for the BPI-SF interference.

Pain duration: Subjects reported the duration since they first experienced the pain they were currently suffering from in the questionnaire. If the pain was not persistent, they reported how often the pain recurred. The number of days since the first pain episode was used as the measure of pain duration if the pain was frequently recurring at least several times a week. If the pain was not frequently recurring several times a week, the number of days of the last pain episode was used as the duration measure (duration range from 90–22,630 days).

Pain persistence: Number of hours a day with pain was assessed by the subjects reporting what percentage of an average day they were in pain. The question was: If all the time is 100%, for what percentage of each day are you in pain?

Number of pain locations: The number of pain regions was registered to agree with the definition of generalised pain [29]. By this definition, the maximum would be 5 body parts (right upper, right lower, left upper, left lower, axial). The number was taken from the marked areas in the pain drawings from the BPI-SF questionnaire and corresponded well with the fibromyalgia diagnosis in all but five cases. In these five pain drawings, there was pain in fewer than four body regions despite the fibromyalgia diagnosis.

The dependent variables

The Hospital Anxiety and Depression Scale (HADS) was used to measure the levels of anxiety and depression in the sample [30]. In HADS, anxiety and depression are both measured using seven different items. For both scales the highest possible score is 21. The lowest possible score is 0. The cut-off score for clinical anxiety is >9 on the anxiety scale and the cut-off score for clinical depression is >7 on the depression scale [31]. The validity of the HAD scale has been reported to be good in primary care patients and the internal consistency has been reported to be good, as well ($\alpha=0.6$) [32].

Power analyses

A power calculation was conducted using G*Power. We aimed to achieve a power level of 95% to be able to detect a moderate effect size ($f^2=0.15$) with an alpha level set to 0.05 (two-tailed). Following these criteria with 6 independent variables in the context of a multiple linear regression analysis, a minimum sample of 146 subjects would be required. For the sub-analyses, a power calculation using G*Power was performed. We aimed to achieve a conventional power level of 80% to be able to detect a moderate effect size ($d=0.5$) with a two-tailed t-test and the alpha level set to 0.05. Following these criteria, a total sample size of 128 subjects would be required (64 subjects for each group).

Data analysis

Both descriptive and inferential statistics were performed in this study to show distribution of the data and testing relationships between variables. Two multiple linear regression analyses using forced entry were conducted to test the relationship between the dependent and independent variables. In the first regression analysis, anxiety was the dependent variable and in the second regression analysis, depression was the dependent variable. For each regression analysis, the independent variables were as follows: pain intensity on the VAS, pain intensity on the BPI-SF, the influence on daily activities on the BPI-SF, pain duration, pain persistence, and number of pain locations. Gender and medication were entered in the model to control for these factors. Prior to regression analysis an inferential statistic (independent-samples t-test) was performed to compare the level of depression and anxiety among 1) participants with fibromyalgia syndrome, 2) participants with other musculoskeletal pain diagnoses, 3) participants with low pain intensity and 4) participants with high pain intensity. The cut off point for pain intensity was set as the level of 4 on the VAS.

Results

In total, 189 subjects participated in this study. The majority of the study subjects were female (87.3%) and the mean age of the population was 51.39 years ($SD=14.77$). Among the subjects, 55% ($n=104$) had completed secondary education and 25.4% ($n=48$) had a higher education degree (see Table 2). The percentage of the subjects who were taking pain-relieving medication was 50.3% ($n=95$).

Table 2: Socio-demographic characteristic of the study participants.

Variable	n=189
Age in year, mean (SD)	51.39 (14.77)
Gender, female n, %	165 (87.3)
Education level n, %	
Elementary	37 (19.6)
High school	104 (55.0)
University	48 (25.4)

Pain-relieving medications used in the sample included different analgesic drugs such as paracetamol, tramadol, co-codamol, anti-inflammatory drugs, opioids, muscular relaxants, anti-epileptics and antidepressant drugs.

Among the subjects, 42.9% (81 subjects, all female) were diagnosed with fibromyalgia syndrome, and 57.1% (108 subjects, 84 female) were diagnosed with other musculoskeletal pain states.

The reported mean pain intensity, (using VAS) was 5.19 ($SD=2.64$) while the pain intensity reported by BPI-SE was 22.25 ($SD=7.38$). Pain influence on daily life was 40.57 ($SD=17.48$). The mean level of anxiety was 8.19 ($SD=5.60$) and the mean level of depression was 6.07 ($SD=4.72$). The detailed information is presented in Table 3. Data related to anxiety and depression level were both positively skewed. However, the skewness index of depression level exceeded values for normal distribution (2.50–3.00). Therefore, distribution of the data was normalized by using Log-transformation prior to the statistical analysis.

The result of the t-test (Table 4) revealed that the anxiety level was significantly higher among subjects who reported high pain intensity ($M=9.49$; $SD=4.53$) and in subjects with fibromyalgia syndrome ($M=10.98$; $SD=5.20$).

The level of depression was also significantly higher among subjects with high pain intensity ($M=3.87$; $SD=3.71$).

Table 3: Distribution of respondents in the form of mean and standard deviation to pain (pain intensity VAS, pain duration, pain persistence %, pain intensity BPI-SF, pain interference with daily activities BPI-SF), anxiety and depression.

Variable	Mean (SD)	min-max
Pain intensity, VAS	5.19 (2.64)	0–9.8
Pain duration (days)	4322.64 (4705.81)	90–22630.00
Pain persistence (%)	74.60 (28.25)	0–100
Pain intensity BPI-SF	22.25 (7.38)	0–40
Pain interference BPI-SF	40.57 (17.48)	0–70
Anxiety	8.19 (5.60)	0–21
Depression	6.07 (4.72)	0–21

Table 4: Comparison of anxiety level among subjects with high (over 4) and low (under 4) pain intensity, and individuals with, (1) fibromyalgia syndrome and, (2) other musculoskeletal pain states.

Variable	n	Mean (SD)	t (df)	p-Value
VAS under 4 level	61	5.46 (4.53)	–4.90 (187)	0.000
VAS over 4 level	128	9.49 (5.60)		
Fibromyalgia syndrome	81	10.98 (5.20)	–6.58 (187)	0.000
Other musculoskeletal pain	108	6.10 (4.95)		

and subjects with fibromyalgia syndrome ($M=8.90$; $SD=4.68$) compared to subjects with lower pain intensity and subjects with other musculoskeletal pain diagnoses (Table 5).

The levels of both anxiety and depression increased according to the number of pain locations reported (Table 6). Subjects with five pain locations had the highest level of anxiety (mean=10.55) and depression (mean=8.63).

A multiple linear regression analysis was conducted for each of the dependent variables, anxiety and depression. No multicollinearity in the data in any of the regression analyses was observed with no correlation reaching the $r<0.8$ [33]. Multicollinearity between two or more variables means that two variables measure the same phenomenon [33]. Predictor, VIF levels for both the multiple regression analyses ranged from 1.218–3.170, and collinearity statistics for tolerance in both multiple regression analyses ranged from 0.315 - 0.821. For the regression analyses with anxiety and depression as the outcome measures, the Durbin-Watson results were 1.950 and 1.840, respectively. The Durbin-Watson test is testing the autocorrelation in the residuals from a regression analysis and the values reported above showed that there was a small positive autocorrelation in this data material [33].

A multiple regression analysis with the dependent variable anxiety and six independent variables (pain intensity on the VAS, pain intensity on the BPI-SF, the influence on daily activities on the BPI-SF, pain duration, pain

persistence, and the number of pain locations) was conducted. Gender and pain-relieving medication were entered into the model to control for these factors. The model was significant ('p value' <0.000) and the model explained 37% of the total variance (adjusted $r^2=0.347$). Thus, the independent variables significantly accounted for 37% of the variability in the anxiety level.

The analysis showed (Table 7) that one independent variable, the influence on daily activities, significantly predicted the level of anxiety (standardised $\beta=0.156$, $t=5.693$, $p<0.000$). Thus, if the amount of influence on daily activities increased by one standard deviation, then the anxiety level increased by 0.156 standard deviations. No significant differences were observed between the subjects diagnosed with fibromyalgia syndrome and other musculoskeletal pain states. Since all subjects with fibromyalgia syndrome were female, the gender variable was excluded from this additional test.

Regarding depression as the dependent variable and the same six independent variables, with gender and medication as control variables, another multiple regression analysis was conducted. The model was significant ('p value' <0.000) and the model explained 65.6% of the total variance (adjusted $r^2=0.431$). Thus, the independent variables accounted for 43.7% of the variability in the depression level.

The analysis showed that the three independent variables: gender, the influence on daily activities and the number of pain locations significantly predicted the amount of depression (see Table 8). Thus, if the amount of influence on daily activities increased by one standard deviation, then the depression level increased by 0.378 standard deviations, and if the number of pain locations increased by one standard deviation, then the depression level increased by 0.263 standard deviations. Depression level was significantly higher among female gender

Table 5: Comparison of depression level among subjects with high (over 4) and low (under 4) pain intensity, and individuals with, (1) fibromyalgia syndrome and, (2) other musculoskeletal pain states.

Variable	n	Mean (SD)	t (df)	p-Value
VAS under 4 level	61	3.87 (3.71)	-4.87 (187)	0.000
VAS over 4 level	128	7.12 (4.81)		
Fibromyalgia syndrome	81	8.90 (4.68)	-7.99 (187)	0.000
Other musculoskeletal pain	108	4.02 (3.60)		

Table 6: Mean anxiety level and mean depression level were higher with more number of pain locations reported.

Number of pain locations	Mean (SD) anxiety level	Mean (SD) depression level
1	5.10 (4.26)	3.26 (2.77)
2	5.69 (5.64)	3.68 (3.96)
3	7.78 (5.01)	5.00 (3.77)
4	8.00 (4.86)	4.78 (3.13)
5	10.55 (5.35)	8.63 (4.69)

Table 7: Regression analysis of anxiety (dependent variable) and predicted pain variables, gender and age.

	Unstandardized coefficients		Standardized coefficients	
	B	SE	Beta	p-Value
Gender-female/reference	0.844	1.101	0.050	0.444
Pain intensity (VAS)	0.243	0.201	0.115	0.230
Pain intensity (BPI-SF)	-0.038	0.080	-0.050	0.635
Pain interference (BPI-SF)	0.156	0.027	0.487	0.000
Pain duration	-2.84	0.000	-0.024	0.714
Pain persistence	-0.010	0.018	-0.051	0.570
Number of pain locations	0.489	0.283	0.141	0.085
Pain-relieving medication	0.493	0.758	0.044	0.516

Table 8: Regression analysis of depression (dependent variable) and predicted pain variables, gender and age.

	Unstandardized coefficients		Standardized coefficients	
	B	SE	Beta	p-Value
Gender-female/reference	-0.135	0.065	-1.034	0.033
Pain intensity (VAS)	0.013	0.012	0.101	0.268
Pain intensity (BPI-SF)	-0.008	0.019	-0.044	0.663
Pain interference (BPI-SF)	0.052	0.011	-0.378	0.000
Pain duration	-2.94	0.000	-0.040	0.517
Pain persistence	0.001	0.011	0.110	0.201
Number of pain locations	0.056	0.017	0.263	0.001
Pain-relieving medication	0.037	0.044	0.054	0.404

($M=6.29$; $SD=4.86$) compare to male gender ($M=4.54$; $SD=3.32$). No significant differences between subjects diagnosed with fibromyalgia syndrome and other musculoskeletal pain states were found.

Discussion

The results showed that the independent variable “the influence on daily activities” independently predicted the variability of the anxiety level and the same variable and “the number of pain locations” variable were independently responsible for predicting the depression level. The results found in this study were in line with previous research where perceived disability, functional status, activity level and pain in more body locations were independently associated with both anxiety and depression [16–18]. However, the results from the multiple regression analysis in this study were not in line with the earlier result that found a relationship between higher pain intensity ratings and higher levels of anxiety and depression [16]. To explore the relationship between pain intensity and the levels of anxiety and depression further we performed a subsequent analysis where we compared high intensity pain (VAS above 4) with low intensity pain (VAS below 4). It was clear from the analysis that the mean levels of both anxiety and depression were significantly higher in the high intensity group. In other words, it should be clear that pain intensity and anxiety, as well as pain intensity and depression, coexist, but that in the regression analysis it could not be shown that the present pain intensity or the pain intensity perceived during the last 24 h could predict the perceived level of anxiety or depression. It could be discussed, that maybe the subjects in this sample did not experience enough high intensity pain (mean VAS score:

5.19, $SD: 2.64$) for this variable to be able to predict any of the outcome variables. In fact, the pain intensity could be regarded as moderate following the cut-off points (3.5–6.4) for pain-intensity-related interference with functioning [27]. The results may have been different had the total mean VAS score in the sample been higher.

We also performed a subsequent analysis of the levels of anxiety and depression in the subjects diagnosed with fibromyalgia syndrome compared to the group with other musculoskeletal disorders. The analysis showed that the levels of anxiety and depression were significantly higher in the subjects with the fibromyalgia diagnosis. The reasons for experiencing high levels of anxiety and depression in fibromyalgia syndrome compared to other musculoskeletal diagnoses could possibly depend on factors such as the pain intensity level but an alternative could also be the unclear prognosis of the disease. If the fibromyalgia diagnosis was compared to, for example, knee or hip arthrosis which was prevalent in the group with other musculoskeletal disorders, the difference would be that the arthrosis groups generally have a quite clear prognosis and treatment. Even though these subjects experienced daily pain on a long-term basis, they had received the information from health care specialists that when the pain would become too severe, a total knee or hip arthroplasty would be possible. It could be that the mere knowledge of this treatment option could reduce anxiety and depression levels, at least to some extent.

From the results of this study, where a negative influence of one’s daily activities could predict the variability of anxiety and depression levels, it could be argued that the feeling of being unable to do meaningful activities due to chronic pain may be an important factor affecting the level of anxiety and depression. In pain clinics, treatment usually takes a holistic view, and in this treatment paradigm it is of great importance to know to what extent different pain variables increase the burden of living with chronic pain. Feelings of anxiety and depression have been shown to reduce the quality of life, and individuals with chronic pain have reported less enjoyment in life due to their chronic pain [34].

Living with chronic pain raises existential questions about life and whether it can be meaningful again despite the pain. It also means that the individuals will have to make changes to their life goals to find a new meaning in life [35]. It has been reported that patients experience significant functional improvement and improvement in anxiety and depression levels after acceptance and commitment therapy where the focus is to increase meaningful activities despite the presence of pain [36].

Combining this report with the results from this study, it could be hypothesised that if the individual with chronic pain does not feel that their pain prevents them from undertaking meaningful activities, either through physical or psychological therapy, or from using functional aids, maybe their quality of life could be increased due to reduced levels of anxiety and depression.

Regarding the number of pain locations, our results revealed that a higher number of painful locations in the body could predict the level of depression. This is in agreement with higher levels found here in the group with the fibromyalgia syndrome diagnosis. It could be that if perceived pain from one part of the body successively spreads to more areas this would heighten the level of that negative feeling. However, this usual spreading of pain in the body which is commonly observed in the clinic could be explained from the mechanisms of plasticity in the central nervous system [37] where the disturbed inhibition from descending tracts has been known to be involved in the spreading of pain in the body. The experienced spreading of pain in the body in chronic pain could also be related to the fact that the individual experiencing chronic pain could be less active in daily living and thus experience pain due to less muscle strength around the joints and altered load of certain body parts due to the original pain. Physiotherapy and physical exercise have indeed been shown to have pain – relieving effects in individuals with chronic pain [38, 39]. It is possible, that if health care professionals pedagogically described the factors influencing the spreading of pain in the body, and physiotherapy interventions were increased as a treatment option, the levels of anxiety and depression could be reduced. This is important, since high levels of anxiety and depression could exacerbate pain. It has been shown that depression and pain severity seem to have a reciprocal relationship [15]. It could be mentioned though, that in this study the levels of anxiety and depression (mean anxiety: 8.19, SD: 5.60; mean depression: 6.07, SD: 4.72) were generally below the values where clinical treatment is considered necessary. We found that female gender predicted a higher level of depression, as well. It could be possible that this effect was pain-related but it is more probable that women simply have a considerably heightened risk for depressive symptoms since this have been evidenced in earlier research [40, 41].

Most subjects in our pain sample suffered from a variety of different musculoskeletal pain states (57.1%) and approximately one third (42.9%) of the sample reported a diagnosis with fibromyalgia syndrome. Despite the fact that the fibromyalgia subjects reported having this

diagnosis from a physician the control over the correctness of this diagnosis was less compared to the rest of the sample and this could be regarded as a limitation in the study. Clearly, the pain sample was heterogenous concerning the diagnoses and other pain variables but this is the reality of clinical musculoskeletal pain states. In a research sample, it could have been desirable to have a more homogenous pain sample but since pain perception is complex and dynamic in nature the reality is that all pain samples are actually heterogenous since every pain experience differs between individuals and even in a duration-dependent manner within the same individual [42].

It is important to consider the fact that no causal relationship could be evidenced in this study since we have measured correlations between several different clinical pain variables. However, even though it is not possible to infer causal relationships in clinical correlational studies it could still be important to discuss the relationships of different pain variables and their coexisting factors even if evidence about the direction that the different variables affect each other could not be concluded. In a recently published article, a difference was found between changes in mental health in individuals with pain where individuals experiencing a poorer mental health developed chronic widespread pain to a greater extent than those who did not [43]. It could therefore be argued that anxiety, depression and pain seem to have a reciprocal relationship.

It could also be noted that the group sizes in the sub-analysis between the low-intensity pain group and the high intensity pain group did not reach the required sample size for the 80% power level. Three subjects were missing to reach the acquired sample size in the low intensity group. This is a weakness regarding the analysis of differences in anxiety and depression levels between the high and low intensity pain groups.

In conclusion, the current research contributes to the research within the field of pain and coexistent anxiety and depression. To the best of our knowledge this is the first study to explore the predictive value of the six specified pain variables: present pain intensity, pain intensity during the last 24 h, influence of pain on daily activities, pain duration, pain persistence and number of pain locations on the levels of anxiety and depression. Our results showed that the influence of pain on daily activities significantly predicted the levels of anxiety and that the influence of pain on daily activities and the number of pain locations significantly predicted the levels of depression. In clinical practice, the results could be important to implement in holistic treatment regimens for chronic pain.

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Informed consent: All participants signed an informed consent form.

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