Fear network and pain extent: Interplays among psychological constructs related to the fear-avoidance model

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ABSTRACT

Objective: Psychological constructs related to the fear-avoidance model such as fear of movement, pain catastrophizing, and affective distress have been found to be inter-related among patients with chronic pain. However, relationships of these constructs have mostly been examined using regression-based analyses. This cross-sectional study employs a novel analytical approach, network analysis, to illustrate the complex interplays among these variables as well as pain intensity and pain interference.

Methods: This study utilized the Swedish Quality Registry for Pain Rehabilitation, including data from 10,436 participants (76.0% women; M_age = 45.0 years). Networks were analyzed separately for patients with different pain extents (i.e., numbers of pain locations) as the interplays may differ qualitatively depending on pain extent.

Results: We found that patients with a larger pain extent showed a worse clinical presentation (i.e., more depression and anxiety, increased fear of movement and pain interference), and their network differed from the patients with a smaller number of pain extent in terms of how strongly key variables were interconnected. In all network models, pain interference and catastrophizing showed consistently influential roles.

Conclusion: Our findings highlight the interactive nature of psychological aspects of pain and how interrelated associations differ depending on pain extent. Findings are discussed based on ideas on how both fear and pain become overgeneralized.

1. Introduction

Patients with widespread chronic pain conditions are more likely to experience lower functioning, increased mortality, and poorer quality of life [1–3]. Overgeneralized fear (i.e., to transfer fear to stimuli that is unrelated to an aversive event) has been suggested as a plausible transdiagnostic pathogenic marker of chronic widespread pain, potentially due to anomalies in fear learning (i.e., acquisition and stimulus generalization) [4,5]. It is possible that patterns of associations between fear and pain differ qualitatively for individuals with different degrees of pain extent on the body, indicating the existence of subgroups [6,7]. However, the extent to which these associations differ as a function of pain extent remains to date understudied.

Pain extent refers to the painful areas distributed across one’s body, an important indicator of pain spreading [5]. Compared to other widely used self-perceived pain aspects such as pain intensity and pain interference [8], pain extent focuses more on anatomical experiences and has received insufficient research. While pain extent has been found associated with multiple pain-related perceptions, it is thus far unknown how it moderates these perceptions at a system-level.

The learning process of fear has played an integral role in psychological models of chronic pain in attempt to explain the development and persistence of disability [5,9]. In line with the fear-avoidance model [9,10,11], chronic pain patients’ negative interpretations of their pain can provoke fear of movement, thereby creating a vicious cycle of avoidance, negative affect, and impairment [9,12,13]. Research from both experimental and correlational studies generally provide support to the model, although it has also been subject to multiple refinements over the years due to inconsistent or inconclusive findings [13].

Several psychological factors are involved in this fear-avoidance process. As a key indicator of pain response and disability, pain catastrophizing is usually conceptualized as a process wherein individuals
regard their pain as extremely threatening [9,14]. People with stronger pain catastrophizing thoughts are more likely to experience higher pain intensity and interference, as well as increased negative affect including anxiety and depression [15]. Furthermore, fear of movement is usually captured measuring beliefs and attitudes about the relationship between hurt and harm. Higher scores on fear of movement indicate an excessive and debilitating fear of carrying out activities that are believed to cause injury or reinjury, and have been associated with increased pain disability, both cross-sectionally and longitudinally [16,17].

All the aforementioned psychological variables have complex interplays. In fact, several of the premises in the fear-avoidance model, such as how variables are associated sequentially, have been questioned based on contradictory or inconclusive findings; instead, a growing body of research indicate bidirectional relationships between physiological and psychological processes [18]. For example, while the co-occurrence of negative affect and pain catastrophizing is well-established [19], the specific and directional effects among these concepts are far from being confirmed. The co-exacerbating relationships between pain and affective distress (e.g., depression, anxiety) are also well-established [20,21]. Pain characteristics could also influence the above psychological processes. Pain extent may play an important role here, with studies showing depression, pain intensity, and pain extent to be inter-related [3,22,23]. Experimental studies also suggest that fear-learning processes could be involved in pain spreading [24,25]; thus, fear learning could be a potential pathway to greater pain extent. However, pain extent and fear are also likely be interlinked in mutually reinforcing cycles. Irrespectively of the direction of associations, individuals with widespread pain may exhibit different patterns of pain-related cognitiveness and affective distress, constituting a qualitatively distinct subgroup among chronic pain patients.

Previous studies predominately use regression-based approaches to examine directional relationships among pain-related variables, with few attempts to explore the multifaceted nature of chronic pain by, for example, examining mutually reinforcing cycles among interrelated variables [26,27]. However, as reviewed above, pain-related variables (e.g., pain intensity, interference) and psychological variables may be bidirectional and reciprocal. Network analysis, in contrast, is a promising statistical method to capture the interrelated nature of pain variables using time-intensive longitudinal data, although there is only a nascent interest in pain research field [28,29]. Notably, a recent Swedish study has applied network analysis in pain rehabilitation, highlighting the potential to delineate the overall structure of the pain experience [29].

Network analysis might be especially important when it comes to psychological aspects of pain given the conceptual overlaps of psychological concepts used in pain research [30]. Using network analysis, one could understand system-level interactions among strongly intercorrelated variables and provide measures of relative importance of each variable in these networks. Network analysis also provides an independent perspective as its evaluation is among a range of variables rather than focusing on a single outcome [31]. Another less-used capability in network analysis is the shortest path, which has been recently applied in psychology to establish the predictive effects from one variable to another with consideration of all other variables in the network [32,33]. While promising, the analytical approach has, to our knowledge, not been used to investigate whether psychological networks differ as a function of pain characteristics such as pain extent.

1.1. Research questions

This study aimed to examine the global structural organization of a set of key psychological constructs related to the fear-avoidance model using network analysis in a large-scale national dataset. In line with the fear-avoidance model [9,11], we expected that individuals with a larger pain extent would have higher scores on measures of fear of movement, catastrophizing, depression, and anxiety, as well as pain interference and pain intensity [6]. Furthermore, we investigated the differences in network structures moderated by patients’ pain extent. As network analysis in pain research is a nascent interest, the analysis was exploratory by nature. However, based on the fear-avoidance model we expected a difference in how fear of movement was expressed and related to the other variables in the network among patients with larger pain extent, and given the co-exacerbation of pain experience (pain intensity and interference) and negative affects [21], these intervariable relationships would be stronger among patients with larger pain extent.

2. Methods

2.1. Participants and procedure

The present study includes a sample of adult patients (ranging from 18 to 90 years) from the Swedish Quality Registry for Pain Rehabilitation, a quality assurance register that contains nationwide data on chronic pain. Patients who are referred to a specialist unit usually suffer from chronic pain that cannot be treated at a primary care level; the pain is not malignant and without need for further medical investigations, and without any indicators of other severe underlying disease (for details, see [34]).

The registry is largely based on different self-report data from established scales regarding chronic pain. Most specialized pain rehabilitation units in Sweden are connected to the registry. There are three different occasions when a patient can be assessed. The first time is before their first visit to a physician at a specialized pain rehabilitation unit, while the second and third assessments happen after the rehabilitation program. The current study used data from the first timepoint.

The registry has gone through a few iterations, and the one used in this study contains 10,436 patients (76.0% women; M̅.age = 45.0 years; 43.0% currently employed; 79.0% Swedish born) who had their first visit to a physician between January 2016 and January 2018. During the first visit, participants received information about the registry and connected research, and signed a written informed consent form. This study was approved by the Swedish Ethical Review Authority, 2018–036, EPM dnr: 2019–02167, EPM 2020–02038.

2.2. Measures

The original question items are in Swedish. Demographic variables including age, gender, employment status, and country of birth were assessed.

Pain catastrophizing. The Pain Catastrophizing Scale was used to measure the exaggerated negative mental experience about pain [35]. It is an established scale in English- and Swedish-speaking samples [35,36]. All 13 items were measured on a 5-point scale (never [0] to all the time [4]). A total score was used for this construct, with higher scores meaning stronger tendency to magnify one’s threat of pain.

Fear of movement. The 17-item Tampa Scale for Kinesiophobia [37] was used to assess fear of movement. All items were measured using a 4-point scale (strongly disagree [1] to strongly agree [4]). The Swedish version has shown its scale reliability [38]. A total score was used. Higher scores indicate more perceived fear of physical movements.

Anxiety and depression were based on two subscales from the 14-item Hospital Anxiety and Depression Scale [39], which has been shown as a reliable measure in Swedish context [40]. With total scores of two subscales, higher scores reflect stronger anxiety and depressive symptoms.

Pain intensity and Pain interference are two subscales from the Multidimensional Pain Inventory [8]. The items were assessed with a 7-point scale (never [0] to very often [6]). This inventory has shown good psychometric properties in previous Swedish studies [41]. Average scores were used for these two constructs, with higher values indicating greater levels of pain intensity and interferences.

Pain extent. Participants were asked to select their painful areas (e.g.,
neck, foot) from a list of 36 predefined anatomical areas, with the front and back sides [6]. The number of such areas with pain was used to indicate the pain extent (summed score range from 0 to 36). In the analyses, pain extent was used as a categorical variable based on cluster analysis, meaning that there are between-cluster qualitative differences [42]. This categorical view of pain extent is consistent with previous research practices [6].

2.3. Analysis
To discern the subgroups of pain extent, the two-step cluster analysis [43] was applied based on log-likelihood and Bayesian Information Criterion (BIC), setting 15 as the maximum cluster number given the large sample size. The optimal model was also evaluated by the Average Silhouette metric; a value over 0.50 mirrors a good solution. As a hybrid clustering approach, the two-step cluster analysis is regarded as a robust method to capture heterogeneities of both categorical and continuous variables [44,45].

Network analysis was the primary analytical method employed in this study as our research aimed to capture the interplays among a set of interrelated variables. We estimated a Gaussian graphic model where edges (i.e., lines) represent the regularized partial correlations between pairs of variables after conditioning on all other variables in the network, to illustrate the topology (i.e., global structural organization) and specific roles of each construct in the network [46,47]. We used R-packages 'bootnet' [47] and 'graph' [48] to estimate networks; a Gaussian Markov random field estimation using graphical LASSO was applied, with extended Bayesian information criterion to decide optimal regularization parameter [47]. This procedure, which estimates 100 different models to identify the optimal model in terms of fit well as parsimony, produces a final sparse network that only depicts the strongest partial correlations among variables and thus protects against false-positive associations. Following the output of network analysis, the system-level connections among nodes (i.e., variables in the network) can be visually observed via the colored and weighted edges (i.e., lines connecting the constructs). The thickness of an edge illustrates the magnitude of association among pairwise nodes. A green edge represents a positive association whereas a red one a negative. We also computed three commonly reported centrality values—strength, closeness—betweenness—to delineate the role of nodes in the network [49].

Strength reflects the direct interaction with other nodes, closeness mirrors how quickly a node passes information to other nodes, and betweenness suggests how frequent a node bridge between other node pairs [46]. Highly central nodes in networks are potentially clinically relevant because when they are “activated”, the likelihood that other nodes will also become activated increases due to the magnitude and number of connections that they share with other nodes. Although there are several centrality metrics, our analyses focused on node strength (i.e., how strongly a node is directly linked to other nodes) as this statistical method is the most interpretable in psychological networks (for discussion, see [50]).

In order to compare network across groups with different number of pain locations, the R-package ‘NetworkComparisonTest’ [51] was utilized to examine the discrepancies in topology and edges [52]. This permutation-based test the null hypothesis that two networks have identical overall structure and that all edges have similar connectivity [47]. With bootstrapping-based tests the null hypothesis that two networks have similarity of the networks [47]. With bootstrapping-based tests (samples = 10⁹), high accuracy of estimation and strong stability of strength values were confirmed. All the permutation-based tests were performed with 5,000 iterations in line with previous studies [32]. Since our analysis held a categorical view about pain extent [42], some spurious edges could be formed since pain extent itself is related to the network nodes [54]. As a sensitivity test, we also utilized moderated network models [55] with the original pain extent score as the moderator among the whole sample. We used R-packages ‘mgm’ [56] to examine the interactions between pain extent and other network nodes. Findings from the factor graph were subsequently compared with the cluster-based network models.

Following the algorithm by Dijkstra [57], we further included pain extent to the above network and established two shortest pathways: from fear (pain catastrophizing, fear of movement) to pain extent. Having been used in previous studies [32,33], the shortest pathways illustrate the predictive effects from fear to pain extent with consideration of other network nodes. For transparency, all R-scripts used for analyses are included in the Supplementary Information.

Prior to primary analysis, data distribution and missing data pattern were examined. Based on visual inspection on Q-Q plots, all variables were deemed normally distributed. Most variables had less than 10% of missing values except for fear of movement (48.2%) because this scale was non-compulsory at some clinics; comparing the patients who completed this scale with those who did not, they all showed similar scores on pain interference (t[9948.06] = -0.94, p = .350; Cohen’s d = -0.02), although the completers reported slightly higher scores on pain intensity (t[9947.94] = 3.46, p = .001; Cohen’s d = 0.01). Detailed missing patterns of variables are tabulated in the Supplementary Information.

Between-clusters comparisons on continuous variables were examined with independent t-tests, along with Cohen’s d estimation for effect sizes [58]. Chi-square test was used to compare between-cluster difference on categorical variables. Consistent with previous network analysis practices [32], pairwise deletion was employed.

3. Results

3.1. Generating pain extent clusters
The two-cluster solution was found as the optimal model (Average Silhouette = 0.7). Cluster 1 is composed of patients with large pain extent (n = 4231; pain extent: M/SD = 24.0/5.3, ranged between 17 and 36). Cluster 2 members had smaller pain extent (n = 6205; pain extent: M/SD = 9.0/4.3, ranged between 0 and 16). Consistent with this clustering, the histogram of pain extent also visually indicates a near-binominal distribution, peaking at both 8 and 18 (see the Supplementary Information).

Table 1 shows the comparisons among the two clusters. Cluster 1 members had a worse clinical presentation than Cluster 2 members, with more fear of movement, catastrophizing, depressive and anxiety symptoms, and pain interference and intensity (with effect sizes in the small to moderate range). There were no different age distributions across clusters (t[99786.84] = 0.639, p = .523), although the proportion of women in Cluster 1 was higher than Cluster 2, \[ \chi^2 = 435.88, p < .001, \text{Cramer’s V} = 0.20. \]

3.2. Networks based on pain extent clusters
Two networks were examined based on participants’ pain extent cluster memberships, as shown in Fig. 1 (for edge weights, see the Supplementary Information). As expected, most of the edges represent positive associations, with two exceptions: anxiety-pain interference and depression-pain intensity. Among the strongest edges were the links between pain interference-pain intensity, anxiety-depression, depression-pain interference, and fear of movement-catastrophizing. Most edge weights showed good estimation stability in 10,000 bootstraps except for depression-fear of movement and anxiety-pain intensity (see the Supplementary Information).

Fig. 2 illustrates the centrality of both clusters. Across all centrality metrics, pain interference, catastrophizing, depression, and anxiety showed consistently stronger influence in both networks. Notably, pain interference and catastrophizing were highly central nodes considering their large strength values, reflecting their strong and direct connections.
Informed by the fear-avoidance model, the present study aimed to investigate the complex interplays among a set of pain-related variables. The network analyses revealed several reciprocal relationships between examined variables. Such an interrelated nature of pain-associated cognitions is in line with earlier findings [9,13]. Consistent with our hypotheses, permutation-based tests suggested that the network was distinct between two groups of individuals with different levels of pain extent. However, the overall differences detected were primarily due to the magnitude of connectivity; the overall pattern of interconnections among variables was similar in both groups. Furthermore, pain interference and catastrophizing were identified as influential nodes in all network models.

Pain extent seems to be an important indicator of patients' pain-related fear and anxiety and depressive symptoms [6]. As expected, patients with a larger pain extent would experience severe health and mental problems, as found in existing studies on patients with chronic widespread pain [1,2]. Specifically, the higher levels of depression, anxiety that were found among individuals with more widespread pain [1,2]. Specifically, the higher levels of depression, anxiety that were found among individuals with more widespread pain [1,2].

4. Discussion

We tested gender differences with a network perspective. When men and women patients were compared, the differences in global strength (\( p = .251 \)) and overall network structure (\( p = .064 \)) were found to be nonsignificant. Strength values in both models showed similar patterns.

Table 1
Mean and standard deviation of study variables and their comparisons by clusters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cluster 1 Larger pain extent (n = 4231)</th>
<th>Cluster 2 Smaller pain extent (n = 6205)</th>
<th>Statistic</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>10.5 (4.9)</td>
<td>8.9 (4.7)</td>
<td>( t = 16.49^*** )</td>
<td>( d = 0.33 )</td>
</tr>
<tr>
<td>Depression</td>
<td>10.0 (4.5)</td>
<td>8.8 (4.5)</td>
<td>( t = 13.03^*** )</td>
<td>( d = 0.26 )</td>
</tr>
<tr>
<td>Pain Catastrophizing</td>
<td>28.4 (11.8)</td>
<td>26.3 (11.1)</td>
<td>( t = 8.76^*** )</td>
<td>( d = 0.18 )</td>
</tr>
<tr>
<td>Fear of Movement</td>
<td>39.9 (9.6)</td>
<td>38.9 (9.3)</td>
<td>( t = 3.70^*** )</td>
<td>( d = 0.10 )</td>
</tr>
<tr>
<td>Pain Intensity</td>
<td>4.5 (1.0)</td>
<td>4.0 (1.2)</td>
<td>( t = 23.64^*** )</td>
<td>( d = 0.48 )</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>4.6 (1.0)</td>
<td>4.2 (1.2)</td>
<td>( t = 20.08^*** )</td>
<td>( d = 0.41 )</td>
</tr>
</tbody>
</table>

Demographic variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cluster 1 Larger pain extent (n = 4231)</th>
<th>Cluster 2 Smaller pain extent (n = 6205)</th>
<th>Statistic</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) – M (SD)</td>
<td>44.9 (11.3)</td>
<td>45.0 (12.8)</td>
<td>( t = 0.639 )</td>
<td>( d = 0.01 )</td>
</tr>
<tr>
<td>Women %</td>
<td>86.6%</td>
<td>68.8%</td>
<td>( \chi^2 = 435.88^*** )</td>
<td>( V = 0.20 )</td>
</tr>
</tbody>
</table>

Note. Between-clusters t-tests were used for all variables except for gender. Gender differences were examined using chi-square test. Effect sizes of t-tests and chi-square tests were examined using Cohen’s \( d \) and Cramér’s \( V \), respectively. *** \( p < .001 \).

We used gender differences with a network perspective. When men and women patients were compared, the differences in global strength (\( p = .251 \)) and overall network structure (\( p = .064 \)) were found to be nonsignificant. Strength values in both models showed similar patterns.

(a) Cluster 1 (patients with larger pain extent)

(b) Cluster 2 (patients with smaller pain extent)

Fig. 1. Pain-related fear networks based on two clusters of patients. Note. AN = Anxiety. DE = Depression. CA = Pain Catastrophizing. FM = Fear of Movement. IT = Pain Intensity. IF = Pain Interference. Nodes are grouped into three colors for better interpretation. Blue nodes: affective distress. Red nodes: pain. Yellow nodes: pain-related cognitions. Green edges mean positive partial correlations and red edges show negative partial correlations. Thicker edges reflect higher degrees of partial correlations between the nodes. Asterisks indicate the significantly different edges between clusters. * \( p < .05 \). ** \( p < .01 \). *** \( p < .001 \). The hollow asterisks show the weaker edges, while the solid asterisks reflect the stronger edges.

3.3. Shortest pathways from fear to pain extent by cluster

As shown in Fig. 3, the shortest pathways from pain catastrophizing to pain extent and from fear of movement to pain extent in Cluster 1 both went through pain intensity. In contrast, two different routes were identified in Cluster 2. While pain catastrophizing transmitted to pain extent via anxiety, fear of movement showed a direct link to pain extent.

4. Discussion

Informed by the fear-avoidance model, the present study aimed to investigate the complex interplays among a set of pain-related variables. The network analyses revealed several reciprocal relationships between examined variables. Such an interrelated nature of pain-associated cognitions is in line with earlier findings [9,13]. Consistent with our hypotheses, permutation-based tests suggested that the network was distinct between two groups of individuals with different levels of pain extent. However, the overall differences detected were primarily due to the magnitude of connectivity; the overall pattern of interconnections among variables was similar in both groups. Furthermore, pain interference and catastrophizing were identified as influential nodes in all network models.

Pain extent seems to be an important indicator of patients’ pain-related fear and anxiety and depressive symptoms [6]. As expected, patients with a larger pain extent would experience severe health and mental problems, as found in existing studies on patients with chronic widespread pain [1,2]. Specifically, the higher levels of depression, anxiety that were found among individuals with more widespread pain (with an average of 24.0 pain locations) is consistent with the key notion of...
that such aspects are highly intertwined with pain and may exacerbate physical symptoms. A substantial body of empirical work, for example, shows that elevated symptoms of depression exacerbate physical, social, and psychological problems among individuals with pain [20]. Our network findings, which support a strong direct link between depression and pain interference, particularly among those with more pain locations, contribute to this body of work. Our findings also align with earlier results from studies using cluster analysis among pain patients [60]. Several previous investigations on subgroup identification have noted clusters with relatively higher affective distress problems [60-63]. Although different sets of subgroups were discerned across studies, the elevated status depression and anxiety is constantly observed given their links with both pain and pain-related cognitions.

In addition, our findings highlight the key role of pain interference and catastrophizing. The large strength centrality of pain interference was also found in a previous network analysis study [29]. While both variables were influential in all examined networks, catastrophizing showed a more pronounced role, relative to pain interference, among patients with more pain locations. Indeed, pain catastrophizing is a central tenet of the fear avoidance model, and it has been linked to a variety of negative outcomes. A recent systematic review of 85 studies (N = 13,628) found that catastrophizing is strongly related to disability [64], and our findings underline catastrophizing as an especially important node among individuals with more widespread pain. There are several potential routes by which catastrophizing impacts pain, including, for example, through increasing depressed mood. It is worth noting, however, that catastrophizing had relatively stronger direct associations with both pain intensity and interference when compared to its partial correlation with depression, lending support to the idea that catastrophizing is an independent contributor to pain [65]. It is currently unknown what role fear learning plays in generalization of pain, but these findings could potentially be explained by the imprecision hypothesis [66]. The basic premise is that associative learning mechanisms influence the way pain is encoded, which, in turn, leads to overgeneralization [66]. Pain, which is here primarily viewed as a conditioned response, is then triggered by a wide array of stimuli, leading to a maladaptive process of overprotection.

In addition to the influential role of catastrophizing, the observed edgewise differences accord broadly with these ideas. Most importantly, we observed that Cluster 1 members, who had more pain locations, showed stronger connections between fear of movement and pain intensity, as opposed to Cluster 2 members. As pain extent increases, the vicious cycle between avoidance and pain intensifies, a process similar to the reciprocal relationship between physical deconditioning and lower pain threshold [67]. On the other hand, fear of movement and pain intensity played less influential roles in the network overall, as indicated by the lower centrality strength values for those nodes in both clusters. We also noted that the intensity-interference link was weaker among the group with more pain locations. Drawing on the imprecision hypothesis [66], it is theoretically possible that the weaker link could be a result of decreased precision in how pain is encoded among those with more widespread pain, potentially due to increased and overgeneralized fear. The findings from shortest pathways analysis provided further support for this notion: among patients with more pain locations the link between fear of pain (catastrophizing and fear of movement) and pain extent was not direct but indirect via pain intensity, whereas for those with fewer pain locations, a direct or indirect link via anxiety was observed.

While the strong anxiety-depression and depression-interference links across groups corroborate the comorbidity commonly observed in chronic pain patients [21,68], we also found that the anxiety-depression and anxiety-pain interference as well as depression-pain intensity links were all stronger among patients with fewer pain locations (Cluster 2). A potential explanation to these findings is that anxiety and depression may play a different role when pain becomes overgeneralized. Thus, while increased levels of symptoms of anxiety and depression were observed among those with more pain locations, as pain spreads emotional responses may become less of an important signal for pain responding specifically, making emotional aspects a distinct problem area in this group. Although tentative, this pattern of findings could indicate emotion dysregulation problems among the group with more pain extent, which would necessitate targeted interventions for the emotional comorbidity, as recently emphasized in the field [69].

With multiple analytical approaches, our study brings the categorical or dimensional nature of pain extent into light. Consistent with the previous practices [6], we deemed pain extent as a categorical variable.

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**Fig. 2.** Standardized strength, closeness, betweenness values of two networks.

Note. IF = Pain Interference. CA = Pain Catastrophizing. AN = Anxiety. DE = Depression. IT = Pain Intensity. FM = Fear of Movement.
which indicates qualitatively different phenotypes of patients. This view is supported by the data distribution (i.e., modality) and produced a set of between-cluster and intervariable differences. The sensitivity analysis in the form of the moderated network model (presented in the Supplementary Information), treating the pain extent variable as continuous, also partly replicated the three-way interactions—mostly on the stronger edges. This, overall, suggested that pain extent could be an important moderator. Yet, some differences were not replicated, and additional interactions also emerged. It is, however, important to note that this analysis assumes that pain extent is normal and continuous and skewed variables may cause problems in this analytical model. Thus, given that the pain extent variable was non-normal, findings should be interpreted considering this fact. Still, while our categorial view provides a practical lens for clinicians to understand patients (e.g., the elevated status of depression and anxiety should be considered among patients with more pain sites), future cluster analysis may adopt a nuanced way to consider the cluster formation (e.g., including more indicators for clusters in order to restrict the within-cluster heterogeneities or using clustering methods that can identify clusters that also allow for additional variability within each cluster [70]).

4.1. Strengths and limitations

The main strengths of the study included the large sample size of chronic pain patients who reported on a number of key psychological variables in a clinical context, the novel analytical approach to study the interplays among variables, and network invariance tests across key pain characteristics as well as shortest pathway analysis. With a Swedish national dataset, findings from this study could be generalized to Swedish patients with disabling nonmalignant chronic pain. The main limitation of our study is its cross-sectional and between-person design; thus, further longitudinal designs are needed to validate thedirectionality of edges. The network analyses could, for example, be further extended by using multiple measurements to examine covariation among variables over time within individuals or by combining it with Directed Acyclic Graphs to elucidate the potential causal structure [71]. Intra-individual and idiographic networks that capture dynamic processes over time may be especially relevant for developing personalized treatment targets and precision medicine [72,73]. We identified some weaker edges in our networks in different analyses. Although bootstrapping-based findings suggest that most edge weights are robust, potential spuriousness may exist because the clusters are based on a recodification of the pain extent variable [54]. Since we relied on self-
reported measures, other important aspects of pain may have been overlooked; thus, future studies could consider using behavioral or physiological measures to capture other dimensions of, for example, pain-related fear and specific pain characteristics.

Notwithstanding, the utilization of network analysis, with invariance comparisons in subgroups, is novel in pain research, paving avenues for more advanced process research on how fear-related processes and pain mutually influence one another and both become overgeneralized [74]. Given the findings of our study, which highlight the strong interplays among examined variables, network analysis could be a useful analytical tool in pain research, particularly in studies examining psychological aspects of pain, where conceptual overlap and bidirectional associations among variables are the norm rather than the exception.

Declaration of Competing Interest

Björn Gerdle is since 2020 involved in a collaboration with Pfizer Inc. concerning chronic low back pain and osteoarthritis. All other authors report no financial relationships with commercial interests.

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Appendix A Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ymgmr.2023.100957.

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