OXFORD

Profiles of Risk and Resilience in Chronic Pain: Loneliness, Social Support, Mindfulness, and Optimism Coming out of the First Pandemic Year

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Abstract

Objective. Individuals experience chronic pain differently, not only because of different clinical diagnoses, but also because of differing degrees of influence from biopsychosocial pain modulators. We aimed to cluster patients with chronic pain into distinct subgroups based on psychosocial characteristics and pain intensity, and we subsequently examined group differences in pain-related interference approximately 1 year later. **Methods**. In this observational, longitudinal study, patients with chronic pain (n = 94) completed validated assessments of psychosocial characteristics and pain intensity at the beginning of COVID-19–related social distancing (April to June 2020). One year later (May to June 2021), patients completed a follow-up survey with assessments of pain interference, loneliness, social support, mindfulness, and optimism. **Results**. A cluster analysis, using psychosocial factors and pain intensity, empirically produced three patient groups: 1) *psychosocial predominant* (PSP), characterized by high psychosocial distress and average pain intensity; 2) *pain intensity predominant* (PIP), characterized by average psychosocial distress and high pain intensity; and 3) *less elevated symptoms* (LES), characterized by low psychosocial distress and low pain intensity. At the 1-year follow-up, patients in the PSP and PIP clusters suffered greater pain interference than patients in the LES cluster, while patients in the PSP cluster also reported greater loneliness and lower mindfulness and optimism. **Conclusions**. An empirical psychosocial-based clustering of patients identified three distinct groups that differed in pain interference. Patients with high psychosocial modulation of pain at the onset of social distancing (the PSP cluster) suffered not only greater pain interference but also greater loneliness and lower levels of mindfulness and optimism, which suggests some potential behavioral targets for this group in the future.

Key Words: Chronic Pain; Psychosocial; Loneliness; Mindfulness; Optimism; Clustering; Pain Interference

Introduction

Protocolization vs. Personalization of Care

Although diagnostic categories are a core tenet of clinical care and guide a reasonable range of treatment choices, individuals who share a common diagnosis are not the same, and some might respond more favorably to one treatment than to another. This is perhaps particularly true in the case of chronic pain [1]. In treating a patient, it is important to consider not only the underlying diagnosis (e.g., arthritis) and predominant presumed mechanism (e.g., neuropathic, inflammatory, nociplastic) but also demographic, social, and psychological factors, as these potentially modulate both the degree of pain [2] and how the patient responds to a proposed treatment.

Ultimately, a move toward more personalized medicine will require that distinct treatment choices fit the "person type" as much as the diagnosis [3, 4].

Biopsychosocial Model

To this end, a consideration of the biopsychosocial model of pain in approaching patients is helpful. The biopsychosocial model of pain implicates a broad array of characteristics as important modulators of pain [2, 5], most commonly including factors such as depression, anxiety, emotional distress, pain catastrophizing, and sleep disturbance, as these factors might meaningfully contribute to the development, maintenance, and impact of persistent pain states [6]. Patients with chronic pain report elevated levels of psychosocial distress compared with pain-free controls [7, 8]. Among individuals with chronic pain, the degree of psychosocial distress is also associated with worse pain-related outcomes [9–12]. Several prospective studies have suggested that psychosocial distress could precede and serve to predict the subsequent development of chronic pain [5, 13, 14]. In addition, there is a strong association of psychosocial factors with pain-related physical, mental, and emotional dysfunction [15–18], beyond their association with pain severity.

Pain Patient Clustering

Recognizing the modulatory role of psychosocial factors in pain, researchers have begun to employ systematic measurement of them to understand how psychosocial modulators interact with and potentially predict pain-related outcomes and disability or response to treatment. In particular, cluster analysis can be used to identify different patterns of patient responses and to distinctly subgroup patients whose pattern of responses is similar [19]. Cluster analysis and similar approaches harness sample heterogeneity on measures of interest to understand how these variables operate differently among individuals, as well as the extent to which variables combine within persons [20, 21]. Identifying subgroups has both theoretical and practical clinical implications for better management of pain.

Recently, models using concurrent assessments of psychosocial factors and pain intensity have allowed for a more nuanced understanding of interpatient variability and an improved prediction of pain outcomes. In particular, the addition of psychosocial variables to the derivation of clustering, including negative affect (depression, anxiety), has resulted in the identification of a group that has both relatively high pain intensity and high levels of psychosocial distress. For example, one study clustered patients on the basis of assessments of psychosocial factors (depression, sleep disturbance, fatigue, illness burden) and pain intensity and identified three subgroups. Specifically, the study identified a group characterized by high psychosocial distress and high pain intensity; a group low in pain intensity and sleep disturbance but with average levels of psychosocial distress; and a group high in sleep disturbance, average in pain intensity, and low in psychosocial distress [22]. Other research has also identified a similar subgroup with both high pain intensity and high levels of psychosocial distress [23, 24] and shown that this subgroup in particular tends to report worse pain outcomes (pain-related interference) [22, 25, 26]. Furthermore, there is some evidence that patient demographic characteristics also differ across clusters, such that a higher frequency of women than men have been found within the subgroup characterized by high pain intensity and high psychosocial distress [26].

Taken together, prior research suggests that clustering based on a more complete picture of patients' characteristics allows identification of clinically meaningful groupings, which may have clinical utility in both identifying underlying predominant pain mechanisms and suggesting the most effective treatments for patients presenting with particular characteristics or risk factors. Although prior research has used cross-sectional designs to focus on how pain-related outcomes differ between clusters, it remains unknown how pain-related interference experienced by these subgroups, identified at one time point, could change over time. Additionally, these subgroups have been clustered by a few well-known psychosocial factors that are typically related to pain outcomes, but less work has investigated how these subgroups might then differ by resilience or coping factors, especially during times of heightened distress, such as living with chronic pain.

Coping During the Pandemic and Pain

The social distancing measures used during the coronavirus 2019 (COVID-19) pandemic have led to widespread and prolonged social isolation [27–29]. Investigating factors that could worsen pain's impact during this time of prolonged social distancing among patients with chronic pain might give insight into areas of challenge, resilience, and opportunity for intervention during subsequent rounds of social distancing or in cases of social isolation generally. Patients living with chronic pain might be at variable, but relatively higher, risk of loneliness [30] and have reduced access to social support, both of which could impact pain interference and pain intensity [31, 32], as well as psychological distress [33, 34]. Additionally, psychosocial traits such as mindfulness and optimism could be severely taxed during times of increased stress but are particularly salient to the experience of pain. Dispositional mindfulness is associated with less pain interference and pain intensity [35, 36], as a well as lower levels of psychological distress [35, 37]. Optimism is also inversely associated with pain intensity [38] and psychological distress [39].

The Present Study

In this study, we used cluster analysis to identify distinct subgroups of patients with chronic pain, using commonly

assessed and salient psychosocial characteristics and pain intensity, which were assessed at the beginning of COVID-19–related social distancing from April to June of 2020. On the basis of prior research, we first aimed to identify unique clusters within our sample and hypothesized that the identified clusters would be distinguished by different levels of psychosocial characteristics (depression, sleep disturbance, stress, and catastrophizing) and pain intensity. Second, we aimed to longitudinally investigate the degree of pain-related interference experienced by these subgroups approximately 1 year into social distancing (May to June 2021). Third, we explored whether these identified subgroups meaningfully differed in terms of negative (e.g., loneliness) and positive (e.g., social support, mindfulness, optimism) psychosocial characteristics, assessed 1 year into social distancing.

Methods

Study Design

This was an observational, longitudinal study of adults with chronic pain from Massachusetts. Patients had to be ≥18 years of age, be English speaking, have had self-reported persistent pain for ≥3 months, and be a current Massachusetts resident. Patients were required to currently reside in Massachusetts in an attempt to ensure similar social distancing mandates and a consistent message from local health authorities [40]. Patients were recruited from Rally, a Partners Healthcare online platform, and by contacting patients from previous studies. The Partners Human Research Committee / Institutional Review Board approved this study. Patients interested in participating were first emailed a link to complete an electronic screening questionnaire via REDCap, a secure online database. The screening questionnaire asked interested participants, "Have you had chronic pain for 3 months or longer?," and it asked them to rate the severity of their pain and to identify the type(s) of chronic pain they had (e.g., back pain, fibromyalgia, postsurgical pain, or other). Eligible patients were subsequently emailed a new link to complete the actual study survey. All patients provided electronic informed consent before participating. This multistep process required participants to complete several interactive steps before having access to the actual study survey, as opposed to clicking on a single link from an online platform, to reduce the risk of online bots (rather than patients) completing the online survey.

Patients completed the first survey from April 28 to June 17, 2020 (Time 1) during the early weeks of the COVID-19 pandemic (Supplementary Data Figure S1) [40]. The majority of patients (147/150) indicated that they were willing to be contacted for future studies and were invited to participate in a follow-up survey. Roughly two thirds of patients (n = 94, 64%) completed the second survey approximately a year later from May 21 to June 7, 2021 (Time 2), after 1 year of living in the pandemic. Each survey took approximately 30–45 minutes to complete, and patients received a $20 Amazon gift code for each survey.

Measures

Variables Used for Patient Cluster Derivation

On the basis of previous research [9, 11, 12], we measured four well-known psychosocial modulators of pain interference, several of which have also been used to cluster pain patients [22], as well as pain intensity. All instructions for questionnaires at Time 1 were prefaced with a clarification that participants should answer the questions in the context of the time frame since they had started social distancing.

Pain catastrophizing. The Pain Catastrophizing Scale (PCS) was used to assess the extent to which patients had catastrophic thoughts associated with pain [41]. The PCS consists of 13 items (e.g., "The pain is terrible, and I think it's never going to get any better") rated on a scale from 0 ("not at all") to 4 ("all the time"). All items are summed for a total score, and higher scores indicate greater pain catastrophizing. The PCS has been validated in pain samples [41, 42] and demonstrated adequate reliability in the present study ($\alpha = 0.96$).

Depression. The Patient Reported Outcome Measurement Information System (PROMIS) eight-item depression short form was used to assess depressive symptoms [43]. Each item (e.g., "I have felt helpless") was rated on a scale from 1 ("never") to 5 ("always"). All items are summed for a total score, and higher scores reflect greater depression. The PROMIS depression short form has been validated in pain samples [43] and showed good reliability in the present study ($\alpha = 0.96$).

Stress. The four-item Perceived Stress Scale (PSS) was used to assess the extent to which patients felt their lives had been uncontrollable [44]. Each item (e.g., "Felt that you were unable to control the important things in your life") was rated on a scale from 0 ("never") to 4 ("very often"). Appropriate items are reverse-scored, and all items are summed for a total score. Higher scores indicate greater perceived stress. The PSS demonstrated adequate reliability ($\alpha = 0.73$) and has been used in pain samples [45].

Sleep disturbance. The PROMIS four-item sleep short form was used to assess sleep disturbance [43]. Each item (e.g., "I had difficulty falling asleep") was rated on a scale from 1 ("never") to 5 ("always"). All items are summed for a total score, and higher scores reflect greater sleep disturbance. The PROMIS sleep short form has been validated in pain samples [43] and showed good reliability in the present study ($\alpha = 0.87$).

Pain intensity. The Brief Pain Inventory (BPI) was used to assess patients' pain intensity [46]. Three items measured patients' worst, least, and average pain. One item measured patients' current pain. All four items were rated on a scale from 0 ("no pain") to 10 ("worst pain imaginable"). A mean score is computed with all four items, and higher scores reflect greater pain intensity. The BPI pain intensity showed good reliability in the present study ($\alpha = 0.89$) and has been validated in pain samples [47, 48].

Outcomes Compared Between Patient Clusters

Pain interference. Seven items from the BPI assessed the extent to which pain interfered with patients' daily activities (e.g., "walking") [46]. All items were rated on a scale from 0 ("my pain has not interfered at all") to 10 ("my pain has completely interfered"). At Time 1, instructions asked patients to reflect on the interference experienced within the prior day, during social distancing. A total pain interference score was computed by summing all seven items, with higher scores indicating greater pain interference. The BPI interference has been validated in pain samples [47, 48] and demonstrated adequate reliability in the present study ($\alpha = 0.91$) at Time 1. At Time 2, patients again answered the seven-item BPI interference, but they were instructed to reflect on the interference experienced over the prior week. A total pain interference score ($\alpha = 0.94$) was created.

Loneliness. The 20-item UCLA Loneliness Scale questionnaire measured how often patients felt lonely [49]. Each item (e.g., "Feel that you lack companionship") was rated on a scale from 1 ("never") to 4 ("often"). All items were summed for a total score, and higher scores indicate greater feelings of loneliness. The UCLA Loneliness Scale has been used in pain samples [50] and showed good reliability in the present study ($\alpha = 0.95$).

Social support. The Multidimensional Scale of Perceived Social Support (MSPSS) was used to assess patients' perceived social support [51]. The MSPSS consists of 12 items measuring support from family, friends, and significant others (e.g., "I can talk about my problems with my family"). All items are rated on a scale from 1 ("very strongly disagree") to 7 ("very strongly agree"). A total score is created by summing all items, and higher scores reflect greater social support. The MSPSS has been shown to be a reliable measure in pain populations [52, 53] and demonstrated adequate reliability in the present study ($\alpha = 0.94$).

Mindfulness. The 10-item Cognitive and Affective Mindfulness Scale—Revised (CAMS-R) was used to assess patients' nonjudgmental awareness of and attention to experiences in the present moment [54]. Each item (e.g., "I can accept things I cannot change") was rated on a scale from 1 ("rarely / not at all") to 4 ("almost always"). Appropriate items were reverse-coded, and all items were averaged for a total score. Higher scores indicate greater levels of trait mindfulness. The CAMS-R showed good reliability in the present study ($\alpha = 0.82$) and has been demonstrated to be a reliable measure in prior pain samples [45, 53].

Optimism. The 10-item Life Orientation Test-Revised (LOT-R) was used to measure patients' optimism [55]. Each item (e.g., "I'm always optimistic about my future") was rated on a scale from 0 ("strongly disagree") to 4 ("strongly agree"). A total score is created by summing all items, and higher scores reflect higher levels of trait optimism. The LOT-R demonstrated adequate reliability in the present study ($\alpha = 0.79$) and has been used in pain samples [56].

Data Analyses

To investigate Aim 1, a cluster analysis was conducted in SPSS version 28.0 (IBM Corp., Armonk, NY, USA) to identify groups of patients with similar scoring patterns on depression, stress, sleep disturbance, pain catastrophizing, and pain intensity. As this was an empirical and exploratory statistical approach, we did not define a priori the number of emergent clusters. As recommended by Henry et al. [57], a two-step clustering approach was conducted. First, Ward's hierarchical technique with squared Euclidean distance as the similarity–dissimilarity between clusters was used. Examination of the dendrogram and changes in the agglomeration coefficients was used to determine the number of clusters present in the data [58], a method that is suitable for exploratory cluster derivation [59]. Second, an iterative, K-means clustering technique was used with the specified number of clusters determined from the Ward's hierarchical technique. These clustering approaches have previously been used to identify subgroups of pain patients [60, 61]. After subgroups of patients had been identified, chi-squared analyses and analyses of variance (ANOVAs) explored how patients' demographic characteristics differed among the derived clusters.

To address Aim 2, ANOVAs were used to determine whether clusters differed on pain-related interference after participants had lived in the pandemic for 1 year. To address Aim 3, a multivariate analysis of variance (MANOVA) was conducted to determine whether the clusters differed on positive (social support, mindfulness, optimism) and negative psychosocial characteristics (loneliness) 1 year into social distancing. For the MANOVA, cluster membership was entered as the independent variable, and the psychosocial measures were entered as the dependent variables.

Results

Patient Characteristics

Participants had a mean age of 40.8 ± 16.1 years and were predominantly female (79%) and White (82%). Marital status was 53% single / never married, and 84% of participants reported an educational attainment of a college degree or higher. All participants reported at least one type of chronic pain, with 43% reporting more than one type of pain, most commonly back pain (60%), fibromyalgia (23%), postsurgical pain (6%), or "other" pain (63%).

Clustering Patients

Candidate clustering factors (depression, stress, sleep disturbance, pain catastrophizing, and pain intensity) assessed at the beginning of social distancing (Time 1, 2020) were standardized as z-scores. Patients with chronic pain were then clustered by their z-scores on candidate variables. The two-stage clustering approach produced three emergent clusters with distinct patterns of derivative factor scores (Figure 1). Group mean raw scores for each derivative factor are depicted in Supplementary Data Figure S2.

Cluster 1 comprised 28.7% of the sample (n = 27) and on the basis of z-scores was descriptively named the *psychosocial predominant* (PSP) cluster. Patients in this PSP cluster scored relatively high on psychosocial factors (z-scores ranging from 0.86 to 1.42) and reported average

levels of pain intensity ($z = 0.18$). Cluster 2 comprised 27.7% of the sample (n = 26) and was labeled the *pain intensity predominant* (PIP) cluster, as patients scored high on pain intensity ($z = 0.83$) but had average levels of psychosocial factors (z scores ranging from −0.18 to 0.25). Cluster 3 comprised of 43.6% of the sample (n = 41) and was labeled the *less elevated symptoms* (LES) cluster. Patients in the LES cluster scored relatively low on all psychosocial factors and pain intensity (z-scores ranging from −0.62 to −0.84).

Demographic Characteristics of Clusters

Table 1 shows demographic characteristics of patients within each cluster. There were significant differences based on age and income between the three clusters. Patients in the PIP and LES clusters were older than were patients in the PSP cluster. Additionally, patients in the LES cluster reported higher income than patients in the PSP cluster. The three clusters did not significantly differ according to gender, race/ethnicity, marital status, or education.

Pain Interference Across Patient Clusters

To determine whether pain interference differed across the three clusters, ANOVAs were conducted. At Time 1 (May 2020), there was a significant overall difference in pain interference between patient clusters (Table 1; Figure 2). Patients in the LES cluster reported significantly less pain interference than patients in the PSP and
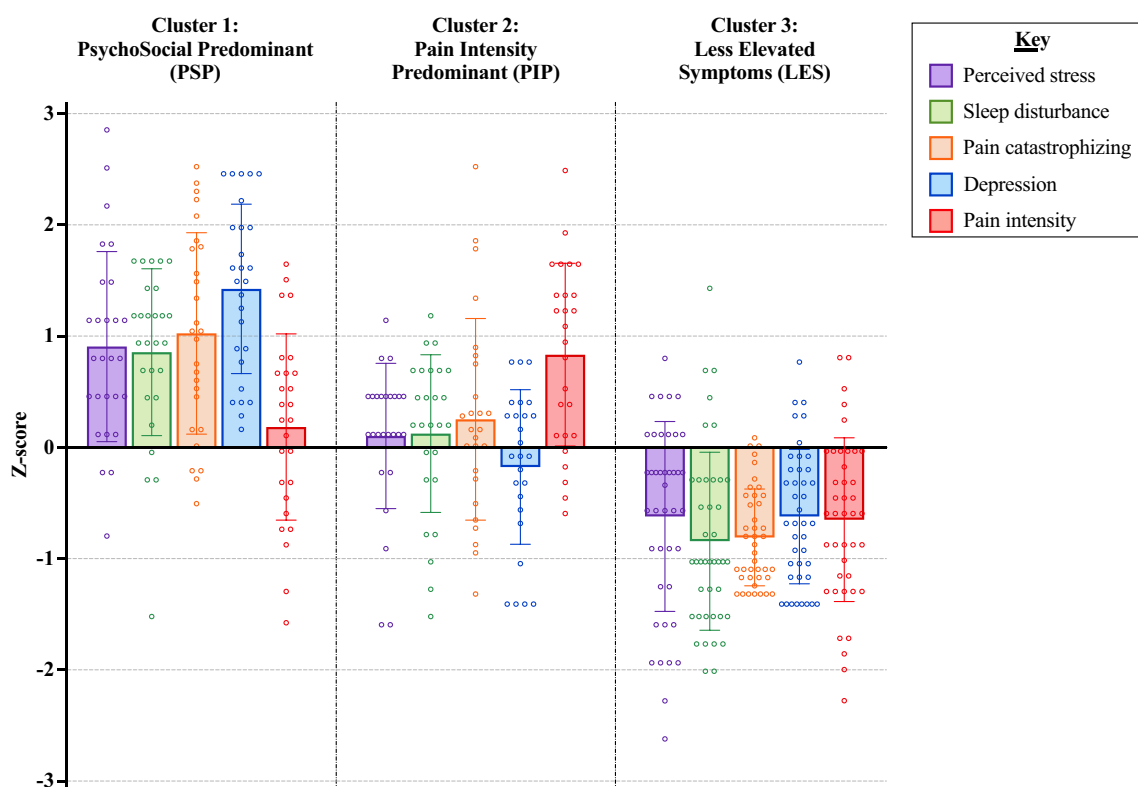

Figure 1. Factor z-scores of three empirically identified subgroups of patients.

Table 1. Demographic, psychosocial, and pain characteristics for the full sample and by patient cluster

Variables	Full Sample Mean (SD) or n (%)	PSP (n = 27) Mean (SD) or n (%)	PIP (n = 26) Mean (SD) or n (%)	LES (n = 41) Mean (SD) or n (%)	P
Demographics					
Age, years *‡	40.83 (16.05)	33.52 (12.91)	43.88 (15.37)	43.71 (17.10)	0.018
Gender					0.052
Male	16 (17%)	3 (11%)	2 (8%)	11 (27%)	
Female	74 (4%)	21 (78%)	23 (89%)	30 (73%)	
Other	4 (4%)	3 (11%)	1 (4%)	–	
Race					0.103
White	77 (82%)	19 (70%)	22 (85%)	36 (89%)	
Black	7 (7%)	1 (4%)	3 (12%)	3 (7%)	
Asian	–	–	–	–	
American Indian	–	–	–	–	
Native Hawaiian / Pacific Islander	–	–	–	–	
Other	9 (10%)	6 (22%)	1 (4%)	2 (5%)	
Prefer not to say	1 (1%)	1 (4%)	–	–	
Ethnicity					0.175
Not Hispanic or Latino	91 (96.8%)	25	36	40	
Hispanic or Latino	2 (2.1%)	2	–	–	
Prefer not to say	1 (1.1%)	–	–	1	
Marital status					0.772
Single, never married	50 (53%)	17 (63%)	12 (46%)	21 (51%)	
Married or in partnership	34 (36%)	7 (26%)	11 (42%)	16 (39%)	
Separated or divorced	6 (6%)	1 (4%)	2 (8%)	3 (7%)	
Widowed	4 (4%)	2 (7%)	1 (4%)	1 (2%)	
Education					0.102
High school	6 (6%)	–	4 (15%)	2 (5%)	
Trade school	4 (4%)	1 (4%)	3 (2%)	–	
Technical/associate's degree	5 (5%)	1 (4%)	1 (4%)	3 (7%)	
Bachelor's degree	46 (49%)	17 (63%)	9 (35%)	20 (49%)	
Graduate/professional degree	33 (35%)	8 (30%)	9 (35%)	16 (39%)	
Income ‡	$50–74,999$_{median}$	$35–49,999$_{median}$	$50–74,999$_{median}$	$50–74,999$_{median}$	0.047
Clustering variables (T1)					
Pain catastrophizing *†‡	17.99 (14.48)	31.71 (12.26)	21.26 (12.28)	6.87 (5.89)	<0.001
Depression *†‡	20.39 (9.10)	31.44 (6.30)	18.19 (5.75)	14.51 (5.00)	<0.001
Perceived stress *†‡	7.71 (2.98)	10.31 (2.50)	7.96 (1.91)	5.85 (2.49)	<0.001
Sleep disturbance *†‡	12.83 (4.25)	16.67 (3.05)	13.69 (2.88)	9.76 (3.25)	<0.001
Pain intensity *†‡	5.06 (1.78)	5.39 (1.49)	6.55 (1.46)	3.90 (1.31)	<0.001
Main outcome variables					
Pain interference (T1) †‡	31.66 (16.57)	42.09 (14.75)	39.16 (12.03)	20.23 (12.67)	<0.001
Pain interference (T2) †‡	27.01 (18.02)	31.63 (16.51)	36.33 (17.62)	18.05 (15.19)	<0.001
Exploratory outcome variables					
Mindfulness (T2) †	2.65 (0.54)	2.42 (0.44)	2.70 (0.61)	2.78 (0.51)	0.018
Optimism (T2) *†	13.28 (4.62)	10.04 (3.82)	13.72 (4.97)	15.15 (3.73)	<0.001
Loneliness (T2) *†	43.48 (10.75)	48.97 (9.39)	42.31 (10.70)	40.61 (10.49)	0.005
Social support (T2)	63.48 (15.97)	57.75 (19.52)	64.19 (16.80)	66.80 (12.65)	0.069

Note. T1 = Time 1 (May 2020); T2 = Time 2 (May 2021). ANOVAs were conducted for continuous variables and chi-squares for categorical variables.

*Significant difference between PSP and PIP clusters ($P < 0.05$).

† Significant difference between PSP and LES clusters ($P < 0.05$).

‡ Significant difference between PIP and LES clusters ($P < 0.05$).

PIP clusters, which had similar levels of pain interference. The pattern of findings was similar for levels of pain interference at Time 2 (May 2021) (see Table 1; Figure 2), despite pain interference being generally lower at this time point.

Exploration of Cluster Characteristics

In addition to assessing differences in pain interference, we explored differences in a set of other salient psychosocial characteristics (loneliness, mindfulness, optimism, and social support) by comparing patients' scores among the three identified clusters of patients after they had lived in the pandemic for 1 year (May 2021). A MANOVA revealed a significant main effect for cluster membership, $F(8,88) = 3.38$, Wilks' $\lambda = 0.75$, $P = 0.001$, partial $\eta^2 = 0.13$. Follow-up ANOVAs revealed a significant group effect for loneliness, mindfulness, and optimism but not for social support (Figure 3).
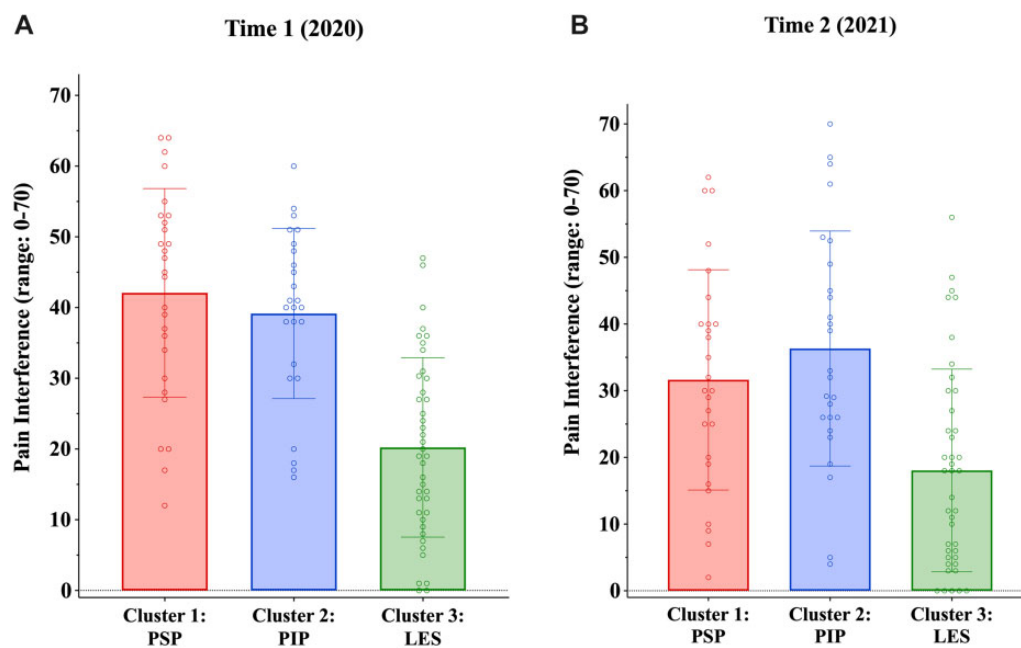
Figure 2. Differences in pain interference among the three patient clusters across time. (A) Patients in the LES cluster reported significantly lower pain interference at Time 1 (May 2020) than either the PSP cluster or the PIP cluster (LES mean $= 20.23 \pm 12.67$ vs PSP mean $= 42.09 \pm 14.75$ vs PIP mean $= 39.16 \pm 12.03$, $P < 0.001$). (B) The LES cluster reported significantly lower pain interference than the PSP and PIP clusters at Time 2 (May 2021) (LES mean $= 18.05 \pm 15.19$ vs PSP mean $= 31.63 \pm 16.51$ vs PIP mean $= 36.33 \pm 17.62$, $P < 0.001$). There were no significant differences in pain interference between the PSP and PIP clusters at either time point.

Post hoc comparisons were then conducted to determine pairwise differences among the clusters on these psychosocial outcomes (Table 1). Patients in the PSP cluster reported greater feelings of loneliness than patients in the LES and PIP clusters. Interestingly, despite these differences in loneliness, there were no significant differences among the three clusters in terms of social support. Patients in the PSP cluster also reported less optimism than the LES and PIP clusters. Patients in the PSP cluster reported lower levels of trait mindfulness than patients in the LES cluster.

Discussion

We used patients' ratings on a set of well-known psychosocial modulators of pain (depression, stress, sleep disturbance, pain catastrophizing) and their pain intensity to empirically characterize distinct clusters within a group of individuals with chronic pain at the beginning of COVID-19 pandemic–imposed social distancing. Three unique subgroups were identified through the use of cluster analysis: PSP, PIP, and LES. The clusters significantly differed in the amount of pain interference they experienced, both at the time of cluster derivation and 1 year later, such that patients in the LES cluster reported lower levels of pain interference than patients in the PSP and PIP clusters. In addition, we found that patients in the PSP cluster reported greater feelings of loneliness and

lower levels of trait mindfulness and optimism 1 year into social distancing. Our findings suggest that patients in the PSP subgroup are at particularly high risk of experiencing a constellation of worse outcomes, including greater pain interference and loneliness and lower optimism and mindfulness.

Previous research has used both self-reported pain intensity [22] and psychophysical assessments of pain sensitivity [25, 26], in combination with psychosocial factors, to categorize patients. Given the socially distanced conditions of the pandemic that prevailed when we conducted these studies, we included pain intensity rather than psychophysical assessments of pain. Thus, patients in our PIP cluster, who reported high pain intensity, might be different from those identified as pain sensitive by psychophysical assessments. However, as in previous studies that used either self-reported pain intensity or formal psychophysical assessments, three clusters emerged, with characteristics approximately similar to those reported previously.

Patients in the LES cluster reported significantly less pain interference than patients in the PSP and PIP clusters. Surprisingly, patients in the PIP cluster, who reported the highest levels of pain intensity (and average psychosocial scores), did not score higher in pain interference than patients in the PSP cluster (who reported average levels of pain intensity but high psychosocial scores). The equivalence of pain interference between these
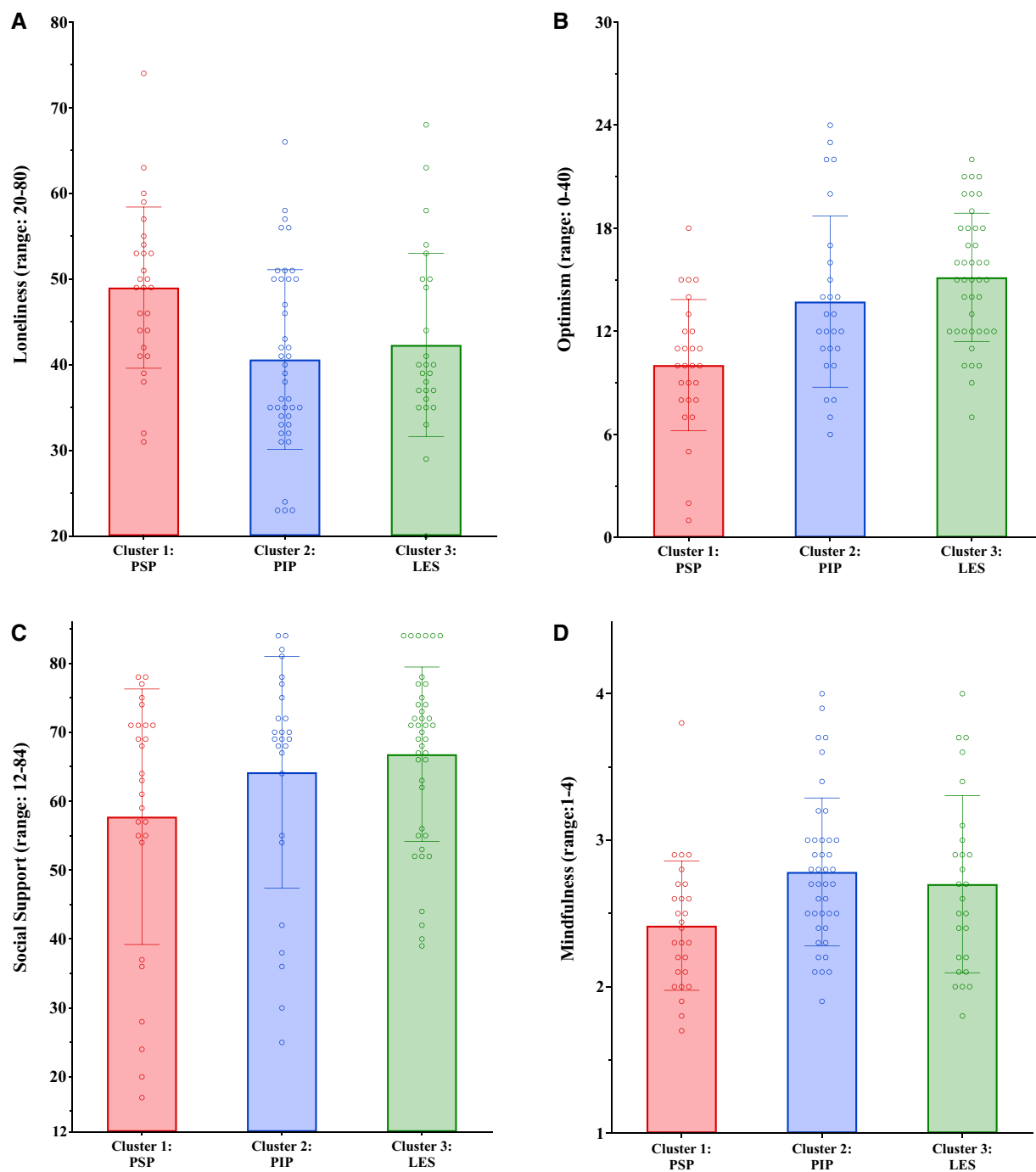
Figure 3. Differences in psychosocial outcomes among clusters 1 year into social distancing. **(A)** There was a significant difference in loneliness between the clusters ($F(2,91) = 5.66$, $P = 0.005$, partial $\eta^2 = 0.111$), with patients in the PSP cluster reporting significantly greater loneliness than that reported by patients in the LES and PIP clusters (PSP mean $= 48.97 \pm 9.39$ vs PIP mean $= 42.31 \pm 10.70$ vs LES mean $= 40.61 \pm 10.49$). There was no significant difference between the PIP and LES clusters. **(B)** There was no significant difference between any of the clusters with regard to perceived social support ($F(2,91) = 2.75$, $P = 0.069$, partial $\eta^2 = 0.057$). **(C)** There was a significant difference in mindfulness between the PSP and LES clusters ($F(2,91) = 4.22$, $P = 0.018$, partial $\eta^2 = 0.085$), with patients in the PSP cluster reporting significantly lower mindfulness than that reported by patients in the LES cluster (PSP mean $= 2.42 \pm 0.44$ vs LES mean $= 2.78 \pm 0.51$). There were no significant differences between the PIP and either the PSP or LES cluster (PIP mean $= 2.70 \pm 0.61$). **(D)** Patients in the PSP cluster reported significantly lower optimism than that reported by either the PIP or LES cluster ($F(2,91) = 12.65$, $P < 0.001$, partial $\eta^2 = 0.218$; PSP mean $= 10.04 \pm 3.82$ vs PIP mean $= 13.72 \pm 4.97$ vs LES mean $= 15.15 \pm 3.73$). There was no significant difference between the PIP and LES clusters.

groups highlights the important modulatory role that psychosocial factors might play in influencing patients' pain interference, in line with the biopsychosocial model

of pain [15–18]. If elevations in the functional impact of pain are driven by different factors in different subgroups (e.g., high pain intensity could be the primary contributor

to pain interference in the PIP subgroup, whereas high levels of psychological distress, poor sleep, and other auxiliary biopsychosocial factors could be stronger contributors to pain interference in the PSP subgroup), this might have important implications for optimizing treatment regimens across subgroups.

We also explored the demographic characteristics of patients in each of the three identified clusters. Patients in the PSP cluster were younger than were patients in the PIP and LES clusters, which identifies younger age as a potential risk factor for both greater pain interference and distress. Indeed, research has shown that younger patients with chronic pain report greater negative affect than do older patients [62, 63]. Additionally, patients in the LES cluster reported higher income than that of patients in the PSP cluster, with potentially more access to resources to better manage their pain and psychosocial distress than those in the PSP cluster had [64, 65].

To gain a deeper understanding of the three subgroups identified, we conducted an exploratory analysis using additional psychosocial characteristics of the subgroups, which we measured approximately 1 year into the pandemic and social distancing. Interestingly, there were no meaningful differences in perceived social support across the three clusters. However, patients in the PSP cluster reported greater feelings of loneliness. Patients in the PSP cluster also reported lower trait levels of mindfulness and optimism. Mindfulness involves awareness and nonjudgment of experiences and is inversely related to psychological distress [37]. Similarly, optimism involves having a positive and hopeful outlook and is associated with less psychological distress [39]. Those who have low levels of trait mindfulness and optimism tend to have negatively biased cognitions (e.g., tendency to interpret negative events as internal or stable) [66], which are associated with negative affective states (depression) and could explain why patients in the PSP cluster scored the lowest on these psychosocial measures. However, more research is necessary to identify directionality in the relationship of these factors.

Phenotypic classification could potentially help clinicians apply personalized interventions based on a patient's characteristics. For example, this could include the determination of differential efficacy in trials of novel therapeutics, which traditionally determine efficacy only in the entire group. Using patient-type stratification might allow more nuanced subgroup testing of novel therapeutics, but it could also give insight into differential mechanisms that are of particular importance within individual patients. This differential testing of novel analgesics could lay the groundwork for a personalized pain medicine approach, where determination of a patient's particular pain phenotype might aid in the decision about what treatment to apply [6, 67]. Several trials of opioid analgesics have noted that elevated pretreatment scores on measures of psychosocial distress (e.g., presumably comparable to the PSP cluster) are associated with reduced opioid analgesic benefit [68–70]. In addition, higher baseline depression scores also predicted higher rates of medication misuse [70]. Similarly, risk factors such as catastrophizing and positive "resilience" factors can independently predict inter-patient variation in the outcomes of multidisciplinary treatment programs; specifically, higher baseline pain resilience was associated with better quality-of-life outcomes, whereas higher baseline catastrophizing was associated with poorer outcomes [71]. Within the perioperative context, there is some evidence that stratifying for high-risk characteristics (such as pain catastrophizing) could allow more sensitive assessment of postsurgical pain prevention by regional anesthesia [72], although future studies are needed to test this principle. It is noteworthy that, in a surgical context, higher catastrophizing is associated with greater benefit from some treatments (e.g., regional anesthesia, open-label placebo) and reduced benefit from other treatments (such as transcutaneous electrical nerve stimulation [TENS]) [73]. Such findings suggest that psychosocial variables, or cluster/subgroup membership based on psychosocial variables, could be important in shaping precision pain medicine approaches.

Limitations and Future Directions

Strengths of this study included the early assessment after the onset of social distancing and the longitudinal design, which allowed assessments of pain-related interference and psychosocial characteristics during a time of social isolation and heightened distress. However, some limitations should be recognized. First, all measures were self-reported online. Future work including laboratory-based psychophysical pain assessment would allow comparison with additional previous cluster solutions. Second, the size of the sample was small, which limits the reliability of the clusters identified and raises concerns about the potential for Type I error in group comparisons. However, previous cluster analyses with small sample sizes (n = 81 patients; e.g., [60]) have proved useful for informing future patient-oriented research. Third, the majority of participants identified as female, White, and highly educated, which limits the generalizability of these findings. Future research will benefit from recruiting a larger, more demographically diverse sample to replicate and strengthen the reliability of the clusters identified. Indeed, researchers have demonstrated differences in catastrophizing and pain-related outcomes reported by White vs Black individuals, as well as women vs men [74–76]. Fourth, although we assessed several social determinants of health, future work should aim to explore how patient clusters might differ on the basis of other social determinants of health, such as occupational status or rurality, particularly among a more demographically diverse sample [77–79]. Fifth, questionnaires were slightly altered at Time 1, with a clarifying clause asking participants to reflect on items with respect to the time frame "since social distancing started" in place of the original language used in each measure (e.g., "in the past

7 days …"), which could impact the ability of questionnaires to be compared with results in previous studies. Lastly, because we did not collect details about the actual social distancing practices followed by each participant, it is possible that the burden was unequally felt among participants. However, all participants resided in the same state, which had relatively tight restrictions and adherence, and participants reported that they experienced a large shift in perceived social isolation, as reported previously [40].

Conclusion

Using systematic brief evaluations of psychosocial factors and pain intensity at the onset of COVID-19–related social isolation, patients with chronic pain clustered into three distinct groups: PSP, PIP, and LES. Patients in the PSP cluster (high psychosocial modulation of pain at the beginning of social distancing) reported the highest levels of pain interference, as well as greater loneliness and lower levels of mindfulness and optimism, after 1 year of social distancing. Understanding and considering which cluster a patient might belong to could help differentially direct targeted therapeutic interventions and inform a more personalized approach to managing pain.

Supplementary Data

Supplementary Data may be found online at http://pain-medicine.oxfordjournals.org.

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