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ORIGINAL RESEARCH

Protective and Risk Factors at the Intersection of Chronic Pain, Depression, Anxiety, and Somatic Amplification: A Latent Profile Approach

ShinYe Kim[1]
Jaehoon Lee[2]
Dianna Boone[3]

[1]Department of Psychological Sciences, Texas Tech University, Lubbock, TX, USA; [2]Department of Educational Psychology, Leadership, and Counseling, Texas Tech University, Lubbock, TX, USA; [3]Center for Behavioral Health, Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA

Objective: Research indicates a complex nexus between chronic pain, depression, anxiety, and somatic amplification (PDAS) symptoms, marked by high rates of co-morbidity and mutually maintaining mechanisms. Although recent frameworks have attempted to explain co-occurrence rates of pain and other comorbid disorders, the interrelations between PDAS and their impacts on pain outcomes have not been adequately examined with a person-centered approach. Using nationally representative data, this study assessed the heterogeneity in PDAS symptomatology and examined links among risk and protective factors in different profiles.

Methods: Data were derived from 1027 participants in the National Survey of Midlife Development in the United States (MIDUS) who completed telephone interviews or self-report measures that assessed PDAS, various sources of social supports (family, friends, spouses/partners, religion, coworkers, and supervisors), and the number of healthcare visits.

Results: We found heterogeneity in symptom *severity* rather than symptom *type* across classes over time. Regardless of comorbidity severity, people reported similar levels of somatic symptoms, which may help clinicians more effectively diagnose comorbidity issues among chronic pain patients. As PDAS symptomatology increased by group, the perceived levels of social support decreased. Membership in a higher symptom severity class was associated with being female, younger age, and an increase in medical, but not mental health visits.

Limitations: Limitations included the use of a cross-sectional design, reliance on self-report measures, and a sample largely comprised of Whites.

Conclusion: PDAS co-occurs across classes, which may relate to shared risk and protective factors. This study lays the foundation to investigate similar questions for overlapping symptoms that occur during the same period, which would shed light on whether—among middle to older age adults—these disorders are attributable to a common mechanism and if they may inform *transdiagnostic* treatments.

Keywords: chronic pain, depression, anxiety, somatic amplification, comorbidity, transdiagnostic

Introduction

Chronic pain, depression, anxiety, and somatic amplification (PDAS) co-occur frequently,[1–5] and people who suffer from chronic pain are more likely to have psychological disorders than those who do not.[2,3] National epidemiological surveys estimate that among those with chronic pain, comorbidity rates between chronic pain and depression range from 5% to 85%[1,6] and approximately 25% of people

Correspondence: ShinYe Kim
Email shinye.kim@ttu.edu

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with chronic pain qualify for a Somatic Symptom Disorder diagnosis.[5] Studies have found that approximately 6%[7] to 35%[8] of those with chronic pain also have a comorbid anxiety disorder, and up to 50% of patients with chronic pain exhibit symptoms of anxiety and depression, although the comorbidity rate exceeds 75% in some studies.[9]

Despite robust evidence for co-occurrence between chronic pain and other psychological disorders, exact mechanisms of development and maintenance of such comorbidity remain ill-defined and controversial in the literature. Recent conceptual models illustrating chronic pain and co-occurring disorders in adolescence have highlighted the dynamic interplay between biological, behavioral, cognitive-affective, and social factors that unfold throughout development.[10] Such factors may interact, potentially predisposing individuals to developing co-occurring pain and depression or maintaining the course of each disorder. For example, due to the lack of positive social interactions, social withdrawal may precipitate depression and exacerbate one's chronic pain. Alternatively, anhedonia or fatigue due to chronic pain or depression could lead to social withdrawal and other forms of behavioral avoidance.[10] Another recent review[11] highlights shared neural pathways and physiological mechanisms that put individuals at risk for developing chronic pain or depression. Specifically, inflammatory processes, dysfunction of stress systems, and shared brain processes associated with pain or depression may influence the onset or exacerbation of the other.[11] Neurobiological mechanisms underlying pain and co-morbid disorders may interact with other psychological or social factors, increasing one's vulnerability to greater or more severe PDAS symptoms.

The diathesis-stress biopsychosocial model of chronic pain[12] depicts that social support from multiple domains, as well as coping strategies, mutually interact with other biopsychosocial factors (eg, genetic disposition, social vulnerabilities and psychiatric conditions) to predict health and pain-related outcomes. PDAS shares multiple protective factors including levels of social support,[13] as well as risk factors, such as being female[14,15] or a racial minority.[16] Notably, people who report co-occurring chronic pain and affective disorders generally experience greater impairment attributable to distress than do those with chronic pain, depression, or anxiety alone.[17] Furthermore, heterogeneity exists among people with PDAS, such that two people with a similar diagnosis may have different symptoms and presentations. As a construct, chronic pain is also highly heterogeneous.[18,19] Identifying subgroups of people is critical to developing individualized preventive strategies and treatment plans. Large comorbidity studies recommend a person-centered approach to discern such subgroups.[20] We assessed not only the degree to which chronic pain and affective disorders co-occur but we also investigated how these associations related to types of social support, sociodemographic variables, and the number of medical vs mental health visits.

Several theories help explain PDAS comorbidity. The shared vulnerability and maintenance model[17] depicts various factors that underlie the development and maintenance of chronic pain and other affective disorders. Cognitive, affective, and neuro-biological mechanisms interact, increasing one's risk of developing both comorbid chronic pain and DAS. For example, one's predisposition to catastrophize (a common presentation of anxiety), may induce fear around activity or exercise, inhibiting one's recovery from injury.[21–23] The model also states that common features of depression-anxiety-somatic amplification may be driving (via meditation/underlying mechanisms) both psychiatric and pain comorbidities. Recent research has highlighted shared neural mechanisms and inflammatory processes, contributing to high rates of comorbidities between pain, depression, and anxiety.[11] As such, chronic pain and DAS share risk and maintenance features, likely interacting in a bidirectional nature, which unfold over time. Similarly, Soltani et al[10] proposed a recent theoretical framework describing links among psycho-social outcomes, neurobiological pathways, and chronic pain. Specifically, this model posits that person-specific factors are related to the bidirectional relation between depression and chronic pain. Soltani et al[10] also emphasized how family social support is related to these person-specific factors.

Another possible theory, the diathesis-stress biopsychosocial model of chronic pain,[12] posits the potential diathesis and psychosocial factors—depression, anxiety, pain sensory catastrophizing or amplification—that contribute to the course and prognosis of chronic pain. A hypothesis of emotion regulation also indicates that chronic pain may result in someone using unhealthy coping skills that fail to improve outcomes and may lead to experiencing more DAS.[4] Finally, the Communal Coping Model of Pain Catastrophizing shifts the focus from the individual to the social level.[24] Specifically, the expression of pain may result in other people's altered expectations, extra assistance, or empathetic responses. Conversely, it is also possible that an exaggerated expression of pain may result

in negative responses from others, which may lead to social rejection and concomitant anxiety and depression.[24]

Assuming homogeneity in the population, several cross-sectional studies that assessed chronic pain and affective disorder comorbidity have relied on factor analyses to determine the relationships among these variables,[25,26] but such variable-oriented approaches are problematic. If, and when, there is heterogeneity in the population, then aggregated results may not apply to individual-based relations, posing the risk of an ecological fallacy.[27] Furthermore, variable-oriented approaches that tailor individual treatments often examine moderators of treatment effects, such as age or problem severity,[28] but have limited ability to simultaneously examine multiple moderators.[29] In contrast, a person-centered approach "… uses multiple indicator variables simultaneously to define subgroups, allowing for more precise matching of subgroups with appropriate treatments".[29] Therefore, person-centered approaches that account for population heterogeneity are recommended.[30,31] One such approach involves Latent Profile Analysis (LPA), which groups individuals into latent homogeneous classes based on similar response patterns across continuous indicators that assess symptom severity.[32] LPA is better suited to examine comorbidity because it will identify whether a proportion of the sample reports chronic pain, depression, or anxiety by themselves or in a combination of all three.

This person-centered approach has been used to examine heterogeneity separately in major depressive disorders,[33] anxiety disorders,[34] non-chronic pain,[35] and chronic pain.[36,37] To our knowledge, only three studies—all of which have some limitations—have conducted LPA on chronic pain and mental health comorbidities.[36–38] First, none examined somatic-related symptoms. Second, the chronic pain subgroups most frequently examined were derived based on pain severity, so it is unclear in what ways mental health issues were related to pain interference. Third, chronic lower back pain was examined most often with less information provided about other chronic pain diagnoses. Fourth, because they frequently focused on risk factors, studies that examined heterogeneity in chronic pain and psychological comorbidities rarely investigated the role of protective factors, such as social support or meditation. Lastly, our understanding is further limited because none of these studies included depression and anxiety items based on clinical interviews.

Consequently, we extended the research to assess heterogeneity in chronic pain-depression-anxiety-somatic amplification symptomatology using nationally representative data. Our study had two goals: 1) examine the best-fitting latent class solution that categorizes participants based on their responses to chronic pain, anxiety, depression, and somatic amplification items; and 2) examine associations among the relevant sociodemographic risk factors, as well as protective factors, frequently associated with group membership. We also examined links between healthcare visits (both medical and mental health) and PDAS in differentiating comorbidity profiles. Research has indicated a link between female gender and higher levels of comorbidity between chronic pain and depression/anxiety.[6,39] There is also a relationship between racial minority status and worse comorbidity patterns,[15] as well as between low social support and higher levels of comorbidity.[40,41] There have been mixed results with respect to age: both younger[16] and older groups[6] have exhibited higher levels of comorbidity.

Methods

Participants and Procedure

We analyzed data from 1,027 participants in the third wave of the National Survey of Midlife Development in the United States (MIDUS), a 2013 national survey of non-institutionalized, English-speaking adults residing in the U.S.[42,43] The study received Institutional Review Board (IRB) approval from the University of Wisconsin–Madison. The MIDUS study, from which the data used in the present study were drawn, performed all procedures involving human protections in accordance with the ethical standards of the University of Wisconsin IRB.

Most sociodemographic variables (except income) were obtained from the baseline phone interviews, whereas most health questions (except subjective health, smoking, and drinking behaviors) were obtained from the self-administered questionnaires.[43] The survey was multimodal, employing an initial 30-minute phone interview followed by a set (two) of questionnaires, which were mailed to individuals after completing the phone interview.[43] Most of the scales that measured psychosocial and health-related outcomes were from the self-administered surveys while demographic information was obtained from the phone interviews. Detailed information regarding data sampling, estimate of sampling, response and selection bias can be found from previous reports in Radler & Ryff[43] and Radler.[44] Participants ranged in age from 25 to 74 (M = 65.2 years, SD = 11.2) with 41.9%

identifying as male and 58.1% as female. Approximately 89.2% identified as White, 3.3% as Black and/or African American, 1.2% as Native American or Alaskan Islander, 0.2% as Asian, 0.1% as Native Hawaiian or Pacific Islander, and 5.0% identified as other races/ethnicities. To enable us to assess employer/colleague support, all study participants were employed and experienced some form of chronic pain. Subjects participated in telephone interviews or completed self-administered questionnaires (IRB approval by the University of Wisconsin), both of which measured behavioral, psychological, and social factors, as well as those related to health and well-being.

Measures

Chronic Pain

To assess for the presence and severity of chronic pain, we first asked the MIDUS screening question: "Do you have chronic pain, that is do you have pain that persists beyond the time of normal healing and has lasted anywhere from a few months to many years?" Those who responded "Yes" were then asked, Brief Pain Inventory (BPI) ["During the past week, how much did your pain interfere with your enjoyment of life"] on a scale of 0 (not at all) to 10 (completely) to assess their pain severity and their score on the BPI interference scale was then calculated.[45] The BPI is an instrument possessing good reliability that assesses the degree to which chronic pain interferes with general activity, walking, work, mood, relationships with others, sleep, and enjoyment of life.[46] Shortened interference scales are frequently used as some items may not apply to all patients.[47] The shortened version was given to all of those in the dataset with chronic pain. Responses were measured on a 10-point scale (0 = not at all, 10 = completely) and based on our sample, the Cronbach's alpha was calculated to be 0.91.

Depression

We assessed depression using a structured clinical interview created by the World Health Organization's Composite International Diagnostic Interview (CIDI).[48] A trained telephone interviewer conducted each structured interview. Although this version of the CIDI is based on the Diagnostic and Statistical Manual of Mental Disorders-3rd edition (DSM-III-R),[49] the criteria for Major Depressive Disorder are identical to those specified in the DSM-V.[50] Participants responded to two yes/no questions that asked, 1) if they experienced depression or sadness for two weeks or greater, and 2) if they have experienced anhedonia for two weeks or greater. Participants who endorsed "Yes" to either question were subsequently asked if they experienced at least five of the following symptoms during the past year: depressed mood or anhedonia (most of the day, nearly every day); decreased or increased appetite; insomnia, fatigue or loss of energy; feelings of worthlessness; concentration problems, and recurrent thoughts of death. The final variable ranged from 0 to 7. Scores between 1 and 7 indicated the range of symptom severity and 0 represented participants who did not have a major depression diagnosis.[51] This scale possesses acceptable validity and reliability,[48] and the interrater reliability was reported to be 0.95. Regarding validity, good diagnostic concordance overall was found between a clinical checklist and CIDI diagnoses (K = 0.84 for depressive disorders).[48]

Anxiety

To assess anxiety, participants also participated in structured interviews based on the WHO CIDI Generalized Anxiety Disorder (GAD) determinations, which were based on definitions and criteria specified in the DSM-III -R.[49] The telephone interview assessed GAD symptoms over the prior 12 months. Participants were asked how often they experienced any of the following symptoms attributable to worry: restlessness, feeling keyed up or on edge, or having considerable nervous energy; irritability; trouble falling or staying asleep; difficulty keeping their mind on what they were doing; trouble remembering things; low energy; tiring easily, or sore/aching muscles. The final variable ranged from 0 to 10 with scores between 1 and 10 representing the range of symptom severity and 0, which represented a negative diagnosis for GAD. Participants rated the frequency of their symptoms using a 4-point numerical rating scale (1 = most days, 2 = about half the days, 3 = less than half the days, 4 = never). The scale's interrater reliability was reported to be 0.96 with strong diagnostic concordance between a clinical checklist and CITI diagnoses (K = 0.76 for anxiety disorders).[48]

Somatic Amplification

The original 5-item somatic amplification scale was used to assess the degree to which somatic symptoms are experienced as intense or uncomfortable.[52] Example items included: "I hate to be too hot or too cold" and "Sudden loud noises really bother me".[52] Participants responded on a 4-point Likert scale, ranging from 1 (not at all true) to 4

(extremely true). Total scores were calculated by averaging responses across items with higher scores indicating greater somatic symptom amplification. As shown in prior studies, the scale has good construct validity and strong positive correlations with psychopathological symptoms, including depression, anxiety, hostility, and somatic symptoms.[52] According to Barsky et al.,[52] the scale displayed adequate internal consistency (Cronbach's α = 72) in a sample of hospitalized patients. Based on our sample, Cronbach's alpha was calculated at 0.54.

Doctor and Mental Health Professional Visits

Both the frequency of medical doctor and mental health professional visits were assessed by a single item. Participants were asked, "How many times during the last 12 months did you see a medical doctor?" and "How many times during the last 12 months did you see a mental health professional?"

Meditation/Relaxation Frequency

The use of meditation/relaxation was assessed by asking respondents,

> In the past 12 months, either to treat a physical health problem, to treat an emotional or personal problem, to maintain or enhance your wellness, or to prevent the onset of illness, how often did you use relaxation or meditation techniques?

Participants answered on a 5-point numerical scale (1 = a lot, 2 = often, 3 = sometimes, 4 = rarely, to 5 = never).

Social Support

Social support was examined for the following relationships: family members (other than spouse or partner), spouses/partners, friends, coworkers, supervisors, and religious congregations. All items were answered on a 4-point Likert scale (1 = a lot, 2 = some, 3 = a little, to 4 = not at all). Higher scores represented higher levels of perceived support.

Family and Friends' Support

Family and friends' support were assessed using four questions: 1) How much do they understand the way you feel about things? 2) How much do they really care about you? 3) How much can you rely on them for help if you have a serious problem? and 4) How much can you open up to them if you need to talk about your worries? According to Walen & Lachman,[53] Cronbach's α reliability coefficients for perceived family support were as follows: non-spouse family = 0.82, friends = 0.88, and spouse = 0.86. Evidence for validity was provided through significant small-to-moderate positive correlations with the life satisfaction and self-reported health.[53] Based on our current sample, the Cronbach's alphas for both the family social and friends social support scales were calculated to be 0.87.

Spouse/Partner Support

Spouse/partner's support was assessed using six items: 1) How much does your spouse really care about you? 2) How much does he or she understand the way you feel about things? 3) How much does he or she appreciate you? 4) How much do you rely on him or her for help if you have a serious problem? 5) How much can you open up to them if you need to talk about your worries? and 6) How much can you relax and be yourself around them? Correlations with family strain, positive/negative mood, and life satisfaction is supportive of construct validity.[53] In a previous study, the Cronbach's α was reported to be 0.92,[54] while based on our current sample, it was calculated to be 0.93.

Supervisor/Coworkers' Support

Coworker support was assessed using two questions: 1) How often do you get help and support from coworkers? and 2) How often are your coworkers willing to listen to your work-related problems? Three questions were asked to measure supervisor support: 1) How often do you get the information you need from your supervisor(s)? 2) How often do you get help and support from your immediate supervisor? and 3) How often is your immediate supervisor willing to listen to your work-related problems? Evidence for validity was provided through significant small-to-moderate correlations with negative affectivity, work-to-family and family-to-work conflict.[55] McDonald's omega[56] for this measure was ω = 0.72.

Religious Support

Religious support was assessed using four questions from the Fetzer Multidimensional Measure of Religiosity for Health Research:[57] 1) If you were ill, how much would people in your congregation help you? 2) If you had a problem or were faced with a difficult situation, how much comfort would people in your congregation be willing to give you? 3) How often do people in your congregation or spiritual community make too many demands on you? and 4) How often do people in your congregation or spiritual community criticize you and the things you do?

Correlation with self-rated health is supportive of construct validity.[58] McDonald's omega[56] based on our current sample was $\omega = 0.72$.

Data Analysis

This study performed a secondary analysis of the MIDUS 3 data. Specifically, we utilized latent profile analysis (LPA) to uncover unobserved heterogeneity among adults with chronic pain.[59] LPA, a person-centered approach, provides several statistical advantages in addition to the theoretical supports described earlier. Unlike variable-centered analyses like regression and factor analysis that group similar variables and items, LPA groups individuals based on shared characteristics that differentiate members of one group from those of other group(s). If these shared characteristics represent a range of well-defined pathological constructs, then the resulting symptoms and risks could characterize adults with chronic pain by the nature and complexity of their clinical presentations. LPA also allows for deeper investigations because it merges continuous dimensionality and categorical subgroups into a single model.[60] Thus, complex interactions among the physical and psychological components of comorbidity can be accounted for simultaneously.

In this study, data analysis proceeded in two stages. In the first, LPA was conducted to identify distinct groups/classes of adults with chronic pain that have similar comorbidity profiles—pain (5 domains: pain interfered with general activity, mood, relations with others, sleep, and enjoyment of life), depression, anxiety, and somatic amplification ("class indicators"). We fitted 1- to 4-class models to determine the number of comorbidity classes. In addition to the class profiles' substantive meaningfulness and theoretical conformity,[61] we considered various diagnostic tests and model fit indices[62] including: 1) entropy,[63,64] the larger the value and closer to 1, the less classification error; 2) Vuong-Lo-Mendell-Rubin[65] likelihood-ratio test (LRT); and 3) adjusted Lo-Mendell-Rubin (aLMR)[66] LRT—a significant p value suggests that the k–1-class model should be rejected in favor of the k-class (current) model; and 4) Akaike Information Criteria (AIC)[67] and 5) sample-size adjusted Bayesian Information Criterion (aBIC)[68]—a lower value suggests a better fitting model. For each model, we used robust (full information) maximum likelihood (MLR) estimation implemented in M*plus* 8.0[69] to address missing data (ie, making use of all data points available) and obtain the parameter estimates and sandwich standard errors that are robust to data's non-normality and non-independence.

Once we identified the optimal number of comorbidity classes, the second stage examined the associations between class membership and theoretically meaningful variables related to comorbidity frequency. Those variables included age, gender, number of times a medical doctor or a mental health professional were seen in the prior 12 months, frequency of using relaxation/meditation techniques during the prior 12 months, as well as support from family, friends, spouses/partners, coworkers, supervisor, and their religious congregation. Specifically, we conducted a t-test or analysis of variance (ANOVA, with post-hoc pairwise comparisons when class difference was significant overall), depending on the number of classes identified, to compare the classes for continuous variables, and Chi-squared or Fisher's exact test for categorical variables. The class comparisons were performed using SAS 9.4.[70]

Results

Study Variables' Descriptive Statistics

Tables 1 and 2 provide the descriptive statistics of the variables analyzed. On average, participants were 65.15 (SD = 11.23) years old, and the majority were female (58.1%) and White (89.2%). Typically, participants experienced mild-to-moderate levels of interference with general activity, mood, relations with others, sleep, and enjoyment of life attributable to their chronic pain. They also reported moderate levels of somatic amplification, but low levels of depression and anxiety. The participants had visited a medical doctor approximately five times and a mental health specialist at least once during the prior 12 months. The majority (70.1%) had never used relaxation or meditation techniques during the prior 12 months, but reported good support from family, friends, spouses/partners, coworkers, supervisors, and their congregations.

Comorbidity Classes

Three classes were identified that best represented the profiles of pain, depression, anxiety, and somatic amplification in 1027 adults with chronic pain. Table 3 presents the diagnostic test results and fit values of the latent mixture models that hypothesize one to four classes. Entropy and LRTs are not available for the case of a single class so that comparisons against the 1-class model could not be made using these statistics. The entropy values greater than 0.80 indicated a good separation of the classes in each model.[63] The results

Table 1 Descriptive Statistics of Study Variables (N = 1027)

Variable	*n*	%/*M*	*SD*
Age	1027	65.15	11.23
Sex			
Male	430	41.9%	
Female	597	58.1%	
Race			
White	916	89.2%	
Black/African American	34	3.3%	
Native American/Alaska Islander	12	1.2%	
Asian	2	0.2%	
Native Hawaiian/Pacific Islander	1	0.1%	
Other	51	5.0%	
Pain interfered with			
General activity	993	3.84	3.13
Mood	980	2.95	2.92
Relations with other people	983	2.21	2.87
Sleep	988	3.63	3.24
Enjoyment of life	993	3.70	3.24
Depression	1027	0.95	2.10
Anxiety	1027	0.22	1.17
Somatic amplification	1015	2.46	0.55
Number of times seeing a medical doctor	1013	4.96	7.16
Number of times seeing a mental health professional	1009	1.79	7.85
Relaxation/meditation frequency			
A lot	31	3.0%	
Often	58	5.6%	
Sometimes	105	10.2%	
Rarely	73	7.1%	
Never	720	70.1%	
Support from			
Family	1003	3.45	0.64
Friends	1007	3.26	0.67
Spouse/partner	687	3.58	0.61
Coworker	391	7.05	1.74
Supervisor	341	10.97	2.89
Religious congregation	566	13.78	1.81

of both VLMR and LMR LRTs suggested that three classes best represented the data (i.e., significant *p* values for the 2- and 3-class models and non-significant *p*-values for the 4-class model). The AIC and aBIC values decreased as the number of classes increased. However, it is known well that both AIC and aBIC tend to overestimate the number of classes.[71–74] Therefore, caution should be used when interpreting any AIC or aBIC value. Considering the superiority of the 3-class model indicated by the entropy and LRTs, we concluded that three classes optimally explained the correlations among the participants' pain, depression, anxiety, and somatic amplification.

The three classes were substantively interpretable and could classify those participants who shared highly distinct comorbidity profiles. As depicted in Figure 1, more than half of the participants (n = 554, 54.1%) were included in the first class and showed low levels of pain, depression, anxiety, and somatic amplification. This class was referred to as *Low Comorbidity*. The second class (n = 320, 31.3%) was characterized by moderate levels of comorbidity and was referred to as *Medium Comorbidity*. The last class, referred to as *High Comorbidity*, accounted for the smallest proportion of the sample (n = 150, 14.6%) and showed high levels of comorbidity.

Class Comparisons

Table 2 provides the results of class comparisons of the theoretically meaningful and comorbidity-related variables. The participants in the *High Comorbidity* class were significantly younger than were those in the *Medium* and *Low Comorbidity* classes (both Bonferroni-corrected $p < 0.05$). The *High comorbidity* class also included significantly more females compared to the other two classes ($p < 0.01$). However, the three classes did not differ with respect to the members' races ($p = 0.09$). During the prior 12 months, the participants in the *High Comorbidity* class had seen a medical doctor most often, followed by those in the *Medium Comorbidity* class and then those in the *Low Comorbidity* class (all three Bonferroni-corrected $p < 0.01$). However, there was no difference in the number of visits to a mental health professional ($p = 0.63$) or the frequency of using relaxation or meditation techniques ($p = 0.31$).

The degree of comorbidity was significantly associated with the level of support from others. Support from the family was the lowest in the *High Comorbidity* class followed by the *Medium Comorbidity* class and then the *Low Comorbidity* class (all three Bonferroni-corrected $p < 0.05$). Participants in the *High Comorbidity* class also reported significantly less support from friends than did those in the *Medium* and *Low Comorbidity* classes (both Bonferroni-corrected $p < 0.05$). Similar results were found for spouse/partner support (both Bonferroni-corrected $p < 0.05$). Support from coworkers and supervisors was significantly greater for the *Low Comorbidity* class than for the *Medium Comorbidity* class (both Bonferroni-corrected $p < 0.05$), while the three classes did not differ with respect to support from their religious congregation ($p = 0.10$).

Table 2 Class Comparisons

Variable	Low Comorbidity		Medium Comorbidity		High Comorbidity		Overall Difference			Post-Hoc Comparison		
	n/M	*%/SD*	*n/M*	*%/SD*	*n/M*	*%/SD*	*F/χ2*	*df*	*p*	Low vs Medium	Low vs High	Medium vs High
Age	65.41	11.56	65.98	10.62	62.45	11.02	5.39	2, 1021	0.005	1.000	0.013	0.005
Sex							10.76	2	0.005			
Male	255	46.0%	126	39.4%	48	32.0%						
Female	299	54.0%	194	60.6%	102	68.0%						
Race									0.094			
White	495	89.4%	293	91.6%	125	83.3%						
Black/African American	19	3.4%	6	1.9%	9	6.0%						
Native American/Alaska Islander	3	0.5%	5	1.6%	4	2.7%						
Asian	2	0.4%	0	0.0%	0	0.0%						
Native Hawaiian/Pacific Islander	1	0.2%	0	0.0%	0	0.0%						
Other	29	5.2%	13	4.1%	9	6.0%						
Number of times seeing medical doctor	3.88	3.83	5.34	6.24	6.96	7.55	21.68	2, 1007	< 0.001	< 0.001	< 0.001	0.008
Number of times seeing a mental health professional	1.41	5.91	1.62	5.44	1.89	3.91	0.47	2, 1003	0.625	1.000	1.000	1.000
Relaxation/meditation frequency							9.41	8	0.309			
A lot	15	2.7%	9	2.8%	7	4.7%						
Often	30	5.4%	19	5.9%	8	5.3%						
Sometimes	45	8.1%	38	11.9%	21	14.0%						
Rarely	45	8.1%	19	5.9%	9	6.0%						
Never	399	72.0%	221	69.1%	99	66.0%						
Support from												
Family	3.54	0.54	3.43	0.65	3.18	0.82	19.45	2, 997	< 0.001	0.029	< 0.001	< 0.001
Friends	3.33	0.63	3.20	0.67	3.10	0.78	8.81	2, 1001	< 0.001	0.014	< 0.001	0.407
Spouse/partner	3.67	0.51	3.52	0.65	3.37	0.82	10.67	2, 683	< 0.001	0.015	< 0.001	0.135
Coworker	7.22	1.61	6.73	1.84	6.88	2.05	3.18	2, 387	0.043	0.047	0.712	1.000
Supervisor	11.32	2.62	10.39	3.15	10.65	3.33	3.66	2, 337	0.027	0.030	0.556	1.000
Religious congregation	13.93	1.73	13.68	1.82	13.49	2.00	2.29	2, 561	0.102	0.438	0.176	1.000

Table 3 Diagnostic Test Results and Fit Values of Latent Mixture Models

Model	Entropy	VLMR (*p*)	aLMR (*p*)	AIC	aBIC
1-class	-	-	-	44,116	44,144
2-class	0.90	0.002	0.002	41,334	41,378
3-class	0.89	0.036	0.037	40,513	40,572
4-class	0.90	0.063	0.066	38,789	38,864

Abbreviations: VLMR, Vuong-Lo-Mendell-Rubin; LRT, likelihood-ratio test; aLMR, adjusted Lo-Mendell-Rubin; AIC, Akaike Information Criteria; aBIC, sample-size adjusted Bayesian Information Criterion.

Discussion

The study assessed discrete patterns of chronic pain, depression, anxiety, and somatic amplification symptoms using LPA. Our results determined that a three-class solution that differed only in symptom severity (low comorbidity-class 1, medium comorbidity-class 2, and high comorbidity-class 3) among middle age and older adults fit best. Furthermore, age, sex, number of times a medical doctor was consulted, and social support were significantly associated with the comorbidity classes.

We found that the best-fitting three-class solution was consistent with prior research on chronic pain, depression, and anxiety,[36–38] although only one of these studies included pain interference as a class indicator[38] and none examined somatic symptoms. Two of the studies included chronic pain patients, but did not include chronic pain level as a class indicator. Our study also differed in its focus on depression and anxiety comorbidity. We extended prior studies' findings by assessing intra- and interclass heterogeneity in chronic pain-depression-anxiety symptom severity rates that were based on clinical interviews (CIDI and DSM). Interestingly, our findings indicated differences across classes only in chronic pain-depression-anxiety-somatic amplification symptom severity rather than the types of symptoms comprising each homogeneous class. Thus, this comorbidity symptomatology presented together regardless of severity, and classes were distinguished only by the severity of chronic pain, depression, anxiety, and somatic symptoms, rather than the presence or absence of specific symptoms. This pattern reflected a high degree of similarity in symptom severity response patterns across these distress disorders. These results are consistent with the shared vulnerability and maintenance model,[17] which asserts cognitive, affective, and neurobiological mechanisms interact, increasing one's risk of developing both comorbid chronic pain and DAS.

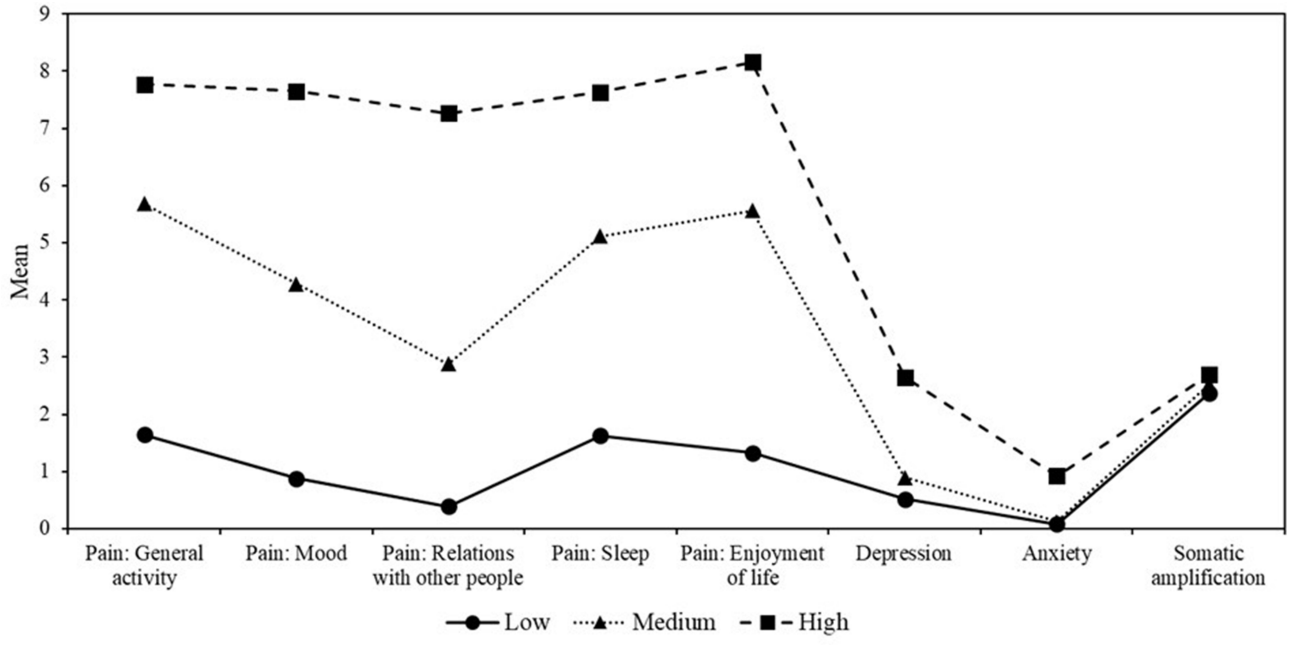

Figure 1 Profiles of three comorbidity classes.

Studies using person-centered approaches to assess symptom heterogeneity, particularly for mood disorders with comorbid chronic pain symptoms, are more limited than variable-centered approaches. Most comorbidity studies to date examined chronic pain and one or two mental health variables. Although there are a few studies (eg)[75–77] that examined PDAS concurrently, all studies on this topic were published around or before 2000 and all of them used a variable-centered approach. To the best of our knowledge, our study is the first person-centered study that examined PDAS comorbidity.

Unlike variable-centered analyses like regression and factor analysis that group similar variables and items, LPA groups individuals based on shared characteristics that differentiate members of one group from those of other group(s). If these shared characteristics represent a range of well-defined pathological constructs, then resulting symptoms and risks could characterize adults with chronic pain by the nature and complexity of their clinical presentation. Also, the use of LPA allows for a deeper investigation because it merges continuous dimensionality and categorical sub-groups into a single model.[60] Thus, complex interactions among the physical and psychological components of comorbidity can be simultaneously taken into account. The use of LPA with symptoms of multiple conditions highlighted important symptom differences (severity and/or type) among sub-classes of people. This finding may inform more individualized clinical assessments and treatments and help us better anticipate that people with severe chronic pain may present with greater levels of depression and anxiety symptoms, either overlapping with chronic pain symptoms or at different times, longitudinally. Therefore, LPA approaches allow for a more refined categorization of individuals.[31]

Our second objective was to ascertain whether differential associations were apparent between chronic pain, depression, anxiety, and somatic amplification groupings and levels of different types of social support. Overall, as the chronic pain-depression-anxiety-somatic symptomatology increased by group, the perceived levels of social support decreased. Specifically, support from family was the lowest in the high comorbidity class, followed by the medium, and then the low. Participants in the high comorbidity class reported significantly less support from friends, as well as from their spouses/partners, than did those in the medium and low comorbidity classes. In particular, coworker and supervisor support was significantly greater for the low comorbidity class compared to the medium class. The three classes did not differ in the religious support they received.

Our findings are consistent with the limited literature that has assessed social support as it relates to co-occurring chronic pain-depression-anxiety symptomatology:[41] an increase in social support was associated with lower levels of comorbidity. At least two explanations can help us understand this. A common explanation is the buffering hypothesis,[78] wherein social support systems help buffer people from adverse effects of stressful events, in this case, chronic pain and psychological comorbidity. Therefore, people who perceive better social support are likely to have lower comorbidity. The Communal Coping Model of Pain Catastrophizing is another framework that can explain the associations between social support and pain comorbidities. Exaggerated expressions of pain may repel people and those with severe comorbidities may be less likely to receive social support. Future longitudinal or experimental studies may help clarify the directional links among social support, chronic pain, and psychological comorbidities.

There are three additional points regarding the symptom patterns. First, people in the low comorbidity class presented with few anxiety symptoms. They did, however, report probable chronic pain and depression diagnoses. This trend is consistent with research that found a greater prevalence of depression than anxiety in chronic pain patients.[2,4,9] Findings from studies that examined chronic pain and psychological comorbidities also shared similar patterns, in which more depressive symptoms (vs anxiety) were associated with chronic pain in comorbidity profiles.[36,37] Second, the level of somatic amplification in the three comorbidity profiles did not differ significantly, indicating that regardless of comorbidity severity, people may report similar levels of somatic symptoms. This information can help clinicians more effectively diagnose comorbidity issues among chronic pain patients along with adding to the literature in which few studies have examined comorbidity among chronic pain, depression, anxiety, and somatic symptoms. Third, chronic pain's comorbidity with anxiety, depression, and somatic amplification increased with class symptom severity. This is consistent with research that has found that, as the severity of chronic pain increases, comorbidity with conditions such as mood disorders also increases.[36,37] People with less severe chronic pain symptoms may also have comorbid depression, psychosomatic issues, and anxiety disorders. They could still benefit from clinical interventions. Therefore, rather than assume that only those people with

more severe chronic pain have mood disorders, those with what appears to be little chronic pain still have psychological comorbidities. Because few studies to date have examined people with less severe comorbidities, further research is needed.

Among sociodemographic risk factors, only sex and age predicted class membership. Being female and younger were associated with membership in a higher symptom severity class. These results are consistent with the existing literature that has reported that being female is a risk factor in chronic pain and psychological comorbidities.[6,39] Our results indicated a significant relationship between younger age and membership in the more symptomatic comorbidity class, a pattern also found in another chronic pain-psychological comorbidity study.[16] While being older is typically associated with greater chronic pain symptoms, older age has also been associated with comorbid chronic pain and depression.[3,15] However, limited research has been conducted to examine the associations among age, chronic pain, and anxiety. Only one study[16] examined the relationship between age and chronic pain-depression-anxiety comorbidities, which found that younger patients were more likely to report pain complaints, depression, and anxiety. The relationships among these variables require further research. Our study contributes to this body of research by providing evidence and explanations of the associations between age and chronic pain-depression-anxiety comorbidities. These results demonstrate that clinicians should consider the importance of certain sociodemographic factors, such as sex and age, and the way they may affect their patients' symptoms relating to comorbid pain and mood disorders.

Racial minority status as a risk factor, along with meditation/relaxation frequency and religious support as protective factors, was not associated with class membership. Similarly, the number of mental health professional visits did not differentiate between classes, although more severe levels of comorbidity symptomatology were associated with an increased number of medical doctor visits. Some studies have examined the number of medical care visits in relation to chronic pain, finding that more severe chronic pain conditions significantly increased the likelihood of frequent healthcare visits.[79] Greater mental health care needs among chronic pain patients were also associated with more frequent healthcare visits.[79] To date, our study is the only one that has examined the associations between the frequency of medical vs mental healthcare visits and chronic pain-depression-anxiety-somatic symptomatology. Our results call for increased attention to the associations between medical/mental healthcare visits and chronic pain comorbidities to optimize healthcare services by focusing on patients with comorbidities who have differing needs.

Limitations and Future Research

Although this study has implications that may contribute to our understanding of, and ability to treat, chronic pain and psychological comorbidity symptoms, it is not without limitations. First, the use of cross-sectional data precludes any conclusions about the direction of effects. For example, among those in the highest comorbidity group, we were unable to determine if low social support leads to greater symptoms or vice versa. Future studies should investigate longitudinal associations among chronic pain, depression, anxiety, and somatic amplification over time. Although using archival data restricted our ability to choose measurements, we believe that the benefit of our data outweighs that weakness because we were able to provide generalizable findings from a nationally representative sample of adults with chronic pain in the United States. In addition, the comorbidity associations between pain interference, depression, anxiety and somatic amplification, as well as how they relate to various types of social support, have not been examined to date, so the present study adds to pain comorbidity research as it relates to psychosocial factors. Additionally, using a nationally representative sample did enable us to generalize our findings to less symptomatic groups. Second, due to using secondary data, we were unable to use well-established measures (eg, somatic amplification and social support), and two of our measures had Cronbach's alpha of 0.54 and 0.57, which are below the 0.70 traditional standard. Future studies should utilize well-validated self-report measures to assess somatic amplification and social support. Third, our sample was primarily older White adults, limiting our ability to generalize the results in other age/racial groups. Fourth, while we used the Brief Pain Inventory to assess pain interference, a single retrospective question was used to discern chronic pain conditions. Due to the subjectivity in chronic pain interpretations, it is possible participants may have under-reported or over-reported their pain symptoms without additional criteria and clinical judgments from healthcare providers. Thus, it will be important for future researchers to conduct follow-up studies with a well-validated clinical interview to reduce the disparities in what constitutes

chronic pain. Lastly, because LPA is primarily an exploratory and data reduction technique, correct class assignments rely on model factors, including covariate effects and sample size,[80,81] making model misspecification possible.

Implications

This study has important clinical and theoretical implications. First, when looking at symptoms of typical comorbid disorders, there seems to be heterogeneity in symptom severity rather than in symptom type across classes over time. Based on the biopsychosocial framework and the body of research in integrative and holistic treatment, assessing risks that may contribute to the development of both pain and psychiatric disorders (based on either demographic or psychosocial factors) significantly enhances provider ability to determine urgency and inform treatment plans and recommendations, especially during triage when not all resources and services are simultaneously available to patients.[12,82,83] Thus, the study findings facilitate practitioners' efficiency to differentiate patients between mild and severe risks for pain and psychiatric comorbidities. For instance, a person who lacks social support, identifies as a younger female, and demonstrates higher levels of DAS is at higher risk, which may warrant more immediate and comprehensive help as compared to others who indicate mild or moderate risk levels. Studies have shown that pretreatment risk assessment to identify who may benefit from a primary care or an interdisciplinary approach is clinically pivotal to treatment outcomes.[12] Patients who received a pretreatment clinical risk assessment reported greater improvements in quality of life and satisfaction compared to those who did not.[84] Clinicians' routine assessment of specific psychosocial outcomes (eg, depression, anxiety, somatic amplification) in addition to pain symptoms will assist clinicians in providing patients with appropriate outpatient mental health referrals. Second, the similarity of types of response patterns across classes supports the idea that chronic pain and mood disorders may share certain risk and protective factors. Third, finding distinct classes of people who differed consistently in symptom severity across symptoms further supports the usefulness of person-centered approaches. Lastly, younger adults, female adults, and adults with less perceived social support may demonstrate more severe comorbidity symptomatology. These variables may be important to address in preventive efforts and should be highlighted in clinical assessments so more tailored treatments can be provided. Encouraging people to build and maintain better social supports may serve as a protective factor for chronic pain, depression, anxiety, and somatic symptom severity.

This study lays the foundation for addressing similar questions about overlapping symptoms during the same period. This will shed light on whether these disorders are attributable to a common mechanism among middle to older age adults and may inform *transdiagnostic* treatments.[85] In conclusion, the study suggests that chronic pain, depression, anxiety, and somatic amplification co-occur, possibly related to shared risk and protective factors. Given this co-occurrence, this study highlighted the need for continual assessment and targeted treatment of co-occurring chronic pain and psychological comorbidities.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding authors on request.

Ethical Approval

The MIDUS study, from which the data used in the present study were drawn, was approved by the University of Wisconsin–Madison IRB and performed all procedures involving human protections in accordance with its ethical standards, as well as the 1964 Helsinki Declaration and its later amendments. Informed consent was obtained from all MIDUS participants. Since the study uses publicly available de-identified data, Texas Tech University IRB office waived the need for additional approval of the study.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

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The authors declare that they have no conflicts of interest for this work.

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