

ORIGINAL RESEARCH

The influence of pain-related comorbidities on pain intensity and pain-related psychological distress in patients presenting with musculoskeletal pain



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KEYWORDS

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Abstract

Background: Musculoskeletal pain (MSP) is the largest contributor to chronic pain and frequently occurs alongside other medical comorbidities.

Objective: Explore the relationships between the presence of pain-related comorbidities, pain intensity, and pain-related psychological distress in patients with MSP.

Methods: A longitudinal assessment of individuals 18–90 years old in the Midwestern United States beginning a new episode of physical therapy for MSP. Electronic medical records were assessed the full year prior to care-seeking of diagnoses for pain-related comorbidities (anxiety, metabolic disorder, chronic pain, depression, nicotine dependence, post-traumatic stress disorder, sleep apnea, and sleep insomnia). Pain intensity and pain-related psychological distress (Optimal Screening for Prediction of Referral and Outcome - Yellow Flags tool) were captured during the physical therapy evaluation. Generalized linear models were used to assess the association between pain intensity, psychological distress, and pain-related co-morbidities. Models were adjusted for variables shown in the literature to influence pain.

Results: 532 participants were included in the cohort (56.4% female; median age of 59 years, Interquartile Range [IQR]:47, 69). Comorbid depression (beta coefficient (β) = 0.7; 95%CI: 0.2, 1.2), spine versus lower extremity pain (β = 0.6; 95%CI: 0.1, 1.1), and prior surgery (β = 0.8, 95%CI: 0.3, 1.4) were associated with higher pain intensity scores. No pain-related comorbidities were associated with pain-related psychological distress (yellow flag count or number of

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domains). Female sex was associated with less pain-related psychological distress ($\beta = -0.2$, 95%CI: $-0.3, -0.02$).

Conclusions: Depression was associated with greater pain intensity. No comorbidities were able to account for the extent of pain-related psychological distress.

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Introduction

Musculoskeletal pain (MSP) has a lifetime prevalence as high as 84%¹ and is the largest contributor to chronic pain,^{2–4} affecting approximately 47% of the general population.⁵ At an individual level, some comorbidities represent medical conditions that can mediate MSP-related health outcomes.⁶ Additionally, physical and mental health comorbidities are present in as many as 50% of individuals with chronic MSP, contributing to the complexity of the management of MSP.⁷ The combination of increased lifespan and prevalence of chronic diseases results in people presenting with multiple comorbidities becoming the norm rather than the exception.⁸ Comorbidities, such as anxiety, metabolic disorder, chronic pain, depression, nicotine dependence, post-traumatic stress disorder (PTSD), and sleep disorders, have all been shown to influence the individual pain experience, patient outcomes, and overall healthcare utilization.^{6,9–16} These comorbidities are often referred to as pain-related comorbidities.^{3,7,17} Considering that comorbidities play a substantial role in the pain experience, a better understanding of relevant comorbidities may improve the treatment of patients with MSP.¹⁸ Accounting for multiple comorbidities is better suited to demonstrate the real world complexity of MSP management. Failure to measure these variables routinely in clinical trials has been identified as one of the key barriers to the proper translation of research findings into clinical practice.¹⁹

Psychological distress, particularly depression and anxiety, has been associated with the development and severity of chronic pain.^{20,21} Many studies identify depression as an influential predictor of pain outcomes.^{22–28} Psychological distress has also been found to predict the persistence of MSP out to one year in other populations in conjunction with comorbidities.^{29,30} Many psychological screening tools focus on vulnerability to pain which includes maladaptive coping strategies and cognitions.³¹ Unidimensional tools may underestimate the full spectrum of psychological distress across multiple domains.³¹ For example, elevated vulnerability to pain may be mitigated by positive resilience factors³²; therefore, both vulnerability and resilience constructs are important in assessing the impact of psychological distress.^{31,33}

A patient's pain experience may be influenced by negative and positive psychological coping factors.³¹ Measuring and understanding multidimensional psychological factors may be important for predicting pain intensity and can be used to assess pain-related psychological distress in individuals with chronic MSP.³⁴ Understanding the influence of person-level comorbidities on pain intensity and pain-related psychological distress may help clinicians consider their management decisions and addressing these comorbidities has the potential to improve MSP clinical outcomes.³⁵

Although the association of mental health comorbidities has been previously investigated,^{28,36–38} multimorbidity models predicting pain intensity and pain-related psychological distress in patients with MSP have not. A better understanding of the association between multiple comorbidities and pain-related outcomes on initial physiotherapy evaluation may improve the timeliness of subsequent referrals and initial management strategies.

The primary aim of this study was to explore the relationship between a history of recent care-seeking for pain-related comorbidities and pain intensity upon initiation of physical therapy for MSP. A secondary aim was to determine the relationship between pain-related comorbidities and pain-related psychological distress. We hypothesized that a recent history of pain-related comorbidities would be associated with greater pain intensity and higher pain-associated psychological distress.

Methods

Study design cohort

A longitudinal assessment using data from electronic medical records (EMR) and claims data from individuals seen in 28 outpatient physical therapy clinics from November 2019 to March 2021 at Bellin Health, a large Midwest health system in the United States. The Bellin Health Institutional Review Board identified the study as exempt and consent deemed unnecessary because routinely collected de-identified health information was used. The Reporting of studies Conducted using Observation Routinely-collected health Data (RECORD) statement was used to guide reporting of this study.³⁹

Data source

De-identified person-level data were extracted for all outpatient visits. The index date was the initial physical therapy evaluation. Self-reported outcomes completed on index date were collected. All medical visits that included International Classification for Disease-Tenth Revision (ICD-10) codes for the entire 1-year before the index date were abstracted, to include those related to the patient's initial MSP diagnosis (list of ICD-10 codes in the [supplementary material](#)).

Participants

Patients were included if they were ages 18–90 years and receiving a physical therapy evaluation for a new episode (defined as no physical therapy in the past year for the same body region) of either neck pain, low back pain, hip

osteoarthritis (OA), or knee OA, (list of ICD-10 codes in the [supplementary material](#)), but the exact acuity of these conditions could not be determined. These musculoskeletal disorders were chosen as they represent common chronic MSP conditions.^{2,40,41} Patients seeking care for pain unrelated to a MSP condition were excluded (e.g., cancer, neurological disease) were excluded.

Descriptive study variables

Patient demographics, including age, sex, race, marital status, and prior history of surgery (either total knee arthroplasty, total hip arthroplasty, and/or any spinal surgery), were identified.

Pain-related comorbidities

The comorbidities of interest included anxiety, metabolic disorder, chronic pain diagnosis, depression, nicotine dependence, PTSD, and sleep disorders, all of which have been identified as potential influencers of MSP outcomes.⁶ For practical purposes, sleep apnea and insomnia were collapsed into a single category of sleep disorders. Comorbidities were identified as medical diagnoses (ICD-10) rendered by a licensed clinician after a care-seeking event in the year before the index date ([supplementary material](#)).

Covariates

Covariates included age, marital status, race, and sex. Other covariates included body region and surgical history in the same body region. Marital status was grouped into three categories based on responses provided by participants at intake: married/cohabitation (married or domestic partner), single/unmarried (single, widowed, divorced, or separated), and unknown (declined or unknown). These demographic variables were chosen for the models because they are known to influence pain intensity or psychological distress.^{41–44} Specifically, marital status has been associated with emotional suffering in chronic pain.⁴⁵ Pain reports can vary by body region.²⁹ Diagnoses for pain in the cervical or lumbar region were collapsed into the classification of spinal region, and diagnoses for hip or knee pain consistent with OA were classified as lower extremity. Surgical history of knee or hip arthroplasty in the same extremity or spine surgery in the same region up to one year prior was identified from the EMR.⁴³

Self-reported outcome variables (taken at index date)

Numeric Pain Rating Scale (NPRS): The NPRS measures pain intensity using an 11-point scale, ranging from 0 (no pain) to 10 (worst pain imaginable).⁴² Patients were asked to rate their average pain over the past week. The 11-point NPRS is considered a reliable, valid, and responsive self-report outcome for patients with MSP.^{43,44}

Optimal Screening for Prediction of Referral and Outcome - Yellow Flags (OSPRO-YF 10): The OSPRO-YF 10 is a reliable and valid tool measuring a multidimensional pain-related psychological distress risk factor profile with 11 distinct flags across three domains.^{29,45} The three domains are: negative

mood (depression, anxiety, and anger), negative coping (beliefs, catastrophizing, kinesiphobia, and pain-anxiety), and positive affect/coping (pain self-efficacy, rehabilitation self-efficacy, and chronic pain acceptance).^{29,45} The term yellow flag describes a psychological factor associated with the pain experience that carries a risk for poorer prognosis.^{31,46,47} However, yellow flags are not synonymous with mental health disorders.³¹ The 10-item version of the OSPRO-YF is standard of care in the clinics and has an 81% accuracy rate compared to the 17-item questionnaire.³¹

Scoring methods for the OSPRO-YF 10 include either a weighted average of the total yellow flag count (11 total possible), a simple summary score (3–53 points), or a total yellow flag domain count (three total possible).³⁰ Scoring the OSPRO-YF tool using either the simple summary score method or yellow flag count has yielded similar predictive accuracy demonstrating good model performance and quality.³⁰ The OSPRO-YF has demonstrated accuracy in predicting 12-month disability, the persistence of chronic pain, risk for subsequent surgery following an episode of physical therapy, and identification of pain and psychological distress phenotypes in patients with hip and knee OA.^{28,29,41}

Data analysis

Generalized linear models were used to determine the relationship between the presence of comorbidities and pain intensity, as well as pain-related psychological distress. Each model was adjusted for the covariates previously defined. The NPRS data were normally distributed and not zero-inflated; therefore, normal identity link was used in the generalized linear model to assess the relationship between pain-related comorbidities and NPRS values. Due to the overdispersion of the OSPRO-YF 10 total yellow flag count variable, a negative binomial family of distributions was used to assess the relationship between pain-related comorbidities and pain-related psychological distress. Negative binomial regression is commonly employed to analyze overdispersed count data by inference based on adjusted score equations for mean and median bias reduction.⁴⁸ A priori significance was chosen at $p < 0.05$ and 95% Confidence Interval (CI) was reported. All variables were assessed for multicollinearity. Only variables with low concern for multicollinearity were retained in the model (based on the correlation matrix, variance inflation factors, and tolerance level estimates). Analyses were completed with SPSS version 28.0 (IBM Corp, Armonk, New York). The best model fit for each analysis was identified using the lowest Akaike's Information Criterion, Bayesian Information Criterion, and most appropriate goodness of fit with Omnibus testing. Variables without a normal distribution are reported with median and interquartile range (IQR).

Sensitivity analysis

As no standard consensus exists yet on the optimal way to clinically interpret the OSPRO-YF 10 results, sensitivity analyses were run using several variations of the pain-related psychological distress measures. In addition to the total count of yellow flags, a model using the OSPRO-YF 10 yellow flags domain count (0 to 3 domains) and another model using the simple summary score were also evaluated

(supplementary material). Finally, as some have recommended treating the NPRS as a count variable due to its ordinal nature and the potential for zero-inflated scores,⁴⁹ we re-ran the analysis using a Poisson distribution instead of the normal identity link.

Results

Of 926 individuals seeking care for spine or lower extremity pain during this period, 532 cases within the age range and with complete OSPRO-YF 10 and NPRS data comprised the final cohort (Fig. 1). None of the covariates or self-reported outcome variables had missing values. PTSD was present in only five cases (0.1% of the cohort) and was not included in any models. Most of the cohort was female ($n = 300$; 56.4%). The overall median age was 59 years, IQR: 47, 69. The median age of individuals with spinal symptoms was 56 years (range: 18–86, IQR: 43, 67) and 67 years (range: 43–85, IQR: 60, 72) for the lower extremity. Most individuals were white ($n = 507$, 95.3%) and married or cohabitating ($n = 331$, 62.2%; Table 1). The mean NPRS for the entire cohort was 5.6 (standard deviation [SD] = 2.2). The mean number of OSPRO-YF 10 yellow flags was 4.7 out of 11 (SD = 3.4), the mean OSPRO-YF 10 simple summary score was 24.8 out of 53 points (SD = 6.2), and the mean number of yellow flag domains was 1.8 out of 3 per individual (SD = 1.0). See supplementary material for specifics. The most frequent pain-related comorbidity was metabolic disorder ($n = 245$, 46.1%; Table 2). Sleep disorders plus metabolic disorder ($n = 28$, 5.3%) were the most frequent co-occurring comorbidities, followed by anxiety plus depression ($n = 21$, 3.9%; Fig. 2).

Pain intensity

Adjusting for all other factors, comorbid depression increased pain intensity by 0.7 points (95%CI: 0.2, 1.2). A

diagnosis in the spine region compared to the lower extremity was associated with an increase in pain intensity of 0.6 points (95%CI: 0.1, 1.1). History of prior surgery was associated with an increase in pain intensity of 0.8 points (95%CI: 0.3, 1.4; Table 3). A sensitivity analysis using a Poisson distribution did not change the results except that spine and lower extremity regions were no longer significant predictors of pain intensity (supplementary material). The data were normally distributed which likely contributed to minimal differences in each model.

Pain-related psychological distress

No pain-related comorbidities were associated with the number of total yellow flags (Table 4). The sensitivity analyses for OSPRO-YF 10 simple summary score and number of domains showed no associations with pain-related comorbidities. The one variable in the model associated with pain-related psychological distress was female sex, showing a small reduction in the total number of yellow flags (0.2 flags; 95%CI: -0.3, -0.02; Table 4). The prevalence of individuals positive for the negative coping domain was different by sex (males $n = 170$; 73.3% and females $n = 199$; 66.3%). Females had 28.1% decreased odds of scoring positive for negative coping compared to males; however, this was not statistically significant (odds ratio [OR]= 0.7, 95%CI: -0.5, 1.1, $p = 0.09$) – supplementary material).

Discussion

The purpose of this study was to determine which pain-related comorbidities were associated with pain intensity and pain-related psychological distress in patients with MSP. In this cohort, depression was the only pain-related comorbidity associated with higher pain intensity scores. Prior surgery or spine pain was associated with higher pain intensity

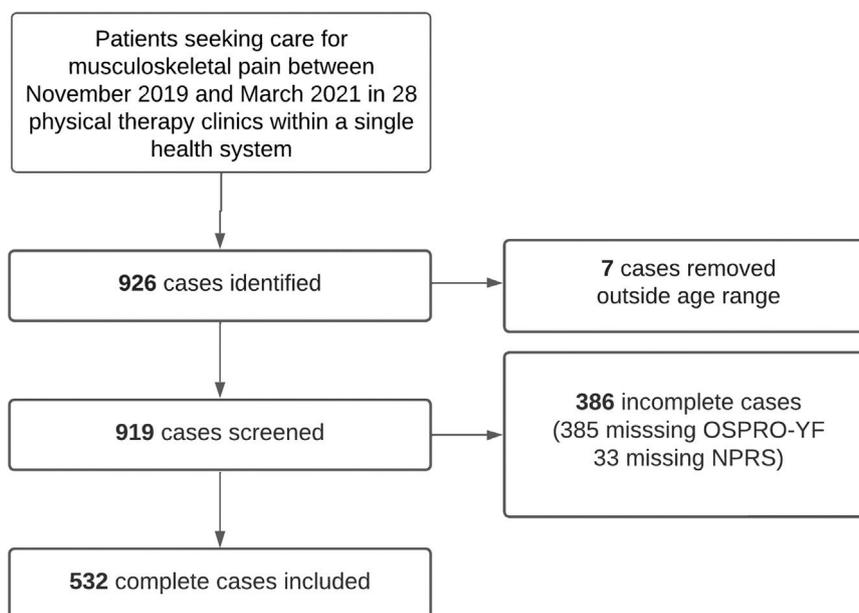


Fig. 1 Cohort inclusion flow chart.

Table 1 Demographics by body region.

Category	Total (n = 532)	Spine (n = 405)	Lower extremity (n = 127)	
Female sex	300 (56.4%)	228 (56.3%)	72 (56.7%)	
Age (median [min-max])	57 [18–86]	56 [18–86]	67 [43–85]	
Race/ ethnicity	White	507 (95.3%)	382 (94.3%)	125 (98.4%)
	Multiracial	5 (0.9%)	4 (1.0%)	1 (0.8%)
	Asian	4 (0.9%)	4 (1.0%)	0
	Black or African American	2 (0.4%)	2 (0.5%)	0
	American Indian/Alaska Native	3 (0.6%)	3 (0.7%)	0
	Unavailable	11 (2.1%)	10 (2.5%)	1 (0.8%)
Marital Status	Married/cohabitation	331 (62.2%)	232 (57.3%)	99 (78.0%)
	Single/unmarried	199 (37.4%)	171 (42.2%)	28 (22.0%)
	Other	2 (0.4%)	2 (0.5%)	0

Table 2 Frequency of pain-related comorbidities by body region and sex.

Comorbidity	Total (n = 532)	Spine (n = 405)		Lower extremity (n = 127)	
		Male	Female	Male	Female
Sex					
Anxiety	93 (17.5%)	26 (14.7%)	52 (22.8%)	4 (7.3%)	11 (15.3%)
Chronic pain	46 (8.6%)	11 (6.2%)	26 (11.4%)	2 (3.6%)	7 (9.7%)
Depression	101 (19.0%)	24 (13.6%)	62 (27.2%)	4 (7.3%)	11 (15.3%)
Metabolic disorder	245 (46.1%)	86 (48.6%)	91 (39.9%)	34 (61.8%)	34 (47.2%)
PTSD	5 (0.9%)	1 (0.6%)	4 (1.8%)	0 (0%)	0 (0%)
Sleep apnea	56 (10.5%)	24 (13.6%)	16 (7%)	8 (14.5%)	8 (11.1%)
Sleep insomnia	43 (8.1%)	15 (8.5%)	22 (9.6%)	0 (0%)	6 (8.3%)
Nicotine dependence	32 (6.0%)	12 (6.8%)	11 (4.8%)	5 (9.1%)	4 (5.6%)

Data are count and percentage; PTSD, post-traumatic stress disorder.

scores. No comorbidities were related to pain-related psychological distress. Female sex was associated with lower pain-related psychological distress. These findings are distinct from other studies in three ways. First, our study explored the relationship between multiple medical comorbidities and pain intensity or pain-related psychological distress rather than a focus on a singular comorbidity. Second, the diagnoses were medically verified through the EMR versus self-report. And third, while most studies report on pain or pain-related psychological distress outcomes after receiving treatment, this study focused on initial patient presentation, unmediated by intervention.

Pain intensity

Depression's association with increased pain intensity corroborates earlier studies investigating depression's impact on pain.^{28,36,37} Accounting for pain-related comorbidities associated with healthcare outcomes and utilization, our results maintained the association of depression with pain intensity while providing new evidence highlighting the relationship at the point of care during an initial physical therapy evaluation.^{6,16,50} Depression and higher pain intensity are prognostic factors in developing chronic low back pain.⁵¹ Likewise, depression is associated with pain intensity and multiple medical comorbidities in patients with knee OA.⁵²

There is likely a bi-directional association between MSP and depression. For example, symptomatic knee OA, in addition to other MSP conditions, have been shown to be associated with a new onset of depression.^{52–55} The impact of not addressing depression throughout an episode of MSP may influence the long-term outcomes for pain intensity and should be considered in further research.

Despite the high prevalence of metabolic disorders in this cohort, a significant relationship between the presence of care-seeking for metabolic disorders and pain intensity was not found. A higher body fat percentage, particularly central adiposity, is associated with developing MSP and is weakly indicative of worsening joint pain.^{56,57} Our study relied on a documented diagnosis of obesity in the medical record, likely representing a high level of variance across the spectrum of obesity. Obesity measures using a continuous variable (e.g., body mass index) may have increased specificity of these relationships but were not available to the research team. We also did not analyze the total number of pain-related comorbidities cumulatively for each individual. It is plausible there is a compounding effect of multiple pain-related comorbidities on pain intensity.

Care-seeking individuals for spine pain were slightly more likely to have increased pain intensity than those care-seeking for lower extremity conditions. To our knowledge, no direct comparison of pain intensity between body regions

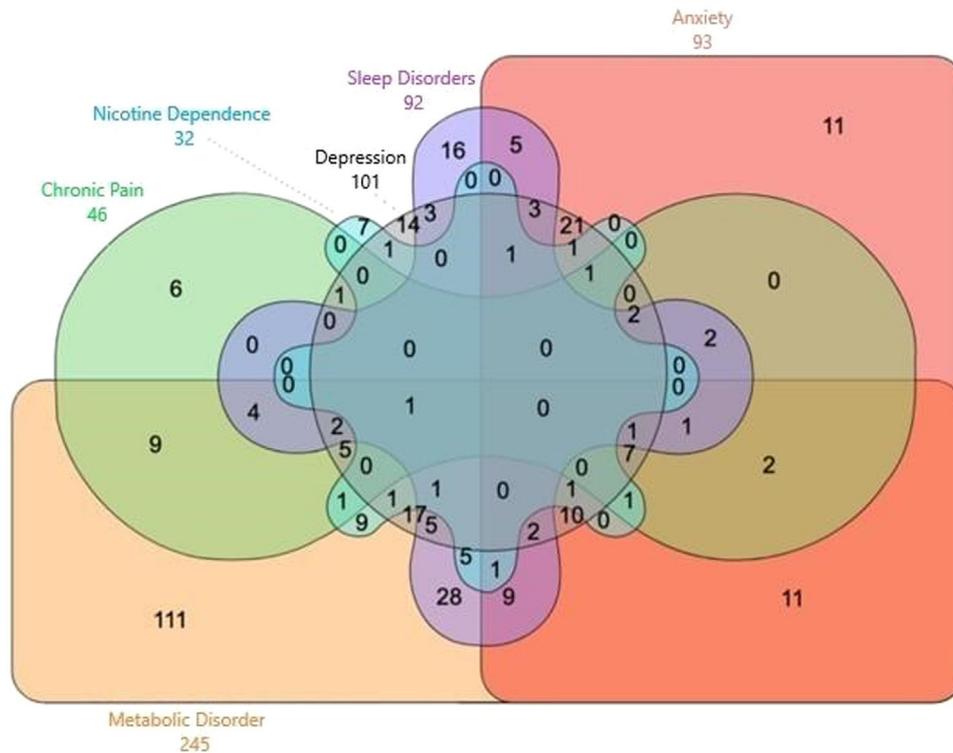


Fig. 2 Interaction of pain-related comorbidities. Venn diagram showing each comorbidity in a different color and the number of patients with the corresponding combinations of comorbidities. ^a Sleep apnea and sleep insomnia were combined into a single category of “sleep disorders”. ^b Post-traumatic stress disorder (PTSD) which had low prevalence ($n = 5$) is not graphically shown, the interactions between PTSD and other comorbidities included: 3 patients with anxiety, depression; 1 with anxiety, depression, chronic pain; 1 with anxiety, depression, chronic pain, sleep disorders (insomnia).

has been made. We offer two potential explanations for this finding. First, individuals with spine pain were younger than those with lower extremity pain. Higher pain intensity is associated with younger age in patients with hip/knee OA.^{58,59} While we adjusted for age in our models, the spine cohort was much larger, making for an unbalanced comparison, and a lack of diversity of ages across both cohorts could limit conclusions. Second, previous studies have suggested that a spatial summation, or how widespread the pain symptoms present, may be a significant determinant of pain

intensity.^{60,61} The referral patterns or indications of spatial summation were not included in this analysis, but future studies exploring relationships between pain-related comorbidities, nociplastic pain, and somatic referral patterns are warranted. However, of noteworthy consideration is the lack of difference in pain intensity across body regions in the sensitivity analysis. Finally, the relationship between a previous history of surgery and pain is consistent with other studies that suggest the possibility of chronic post-surgical pain.^{62–64}

Pain-related psychological distress

The pain-related comorbidities investigated in this study were not associated with pain-related psychological distress. One rationale for this finding may be overlapping characteristics between the items of psychological distress. For example, depression and anxiety occurring concurrently may magnify the level of psychological distress for the individual, but not to the extent necessary to score within the top quartile for the legacy measure required to generate a yellow flag.³¹

Specific factors, including socioeconomic status, type of health insurance, and education level, were controlled for in the original derivation study of the OSPRO YF.³¹ We hypothesize that controlling for these additional factors may have provided more advantageous scores for pain catastrophizing in this cohort. An observable distinction between

Table 3 Parameter estimates for variable association with pain intensity.

Variable	Beta (β)	95% CI	p value
Body region: spine	0.6	0.1, 1.1	0.01
Metabolic disorder	0.3	-0.1, 0.7	0.12
Depression	0.7	0.2, 1.2	0.03
Marital status: married/cohabitation	-0.8	-3.7, 2.1	0.46
Marital status: single/unmarried	-0.2	-3.0, 2.8	0.89
Prior surgery	0.8	0.3, 1.4	0.004
PTSD	1.3	-0.6, 3.2	0.18
Sleep apnea	0.4	-0.2, 1.0	0.19

PTSD, post-traumatic stress disorder.

Table 4 Parameter estimates of variable association with OSPRO yellow flag count.

Variable	Beta (β)	95% CI	p value
Anxiety	0.2	-0.04, 0.4	0.13
Body region: spine	0.2	-0.01, 0.4	0.07
Metabolic disorder	-0.1	-0.3, 0.1	0.19
Chronic pain	0.1	-0.2, 0.3	0.55
Depression	0.1	-0.1, 0.3	0.22
Female	-0.2	-0.3, -0.02	0.03
Marital status: married/cohabitation	-0.2	-1.4, 0.9	0.75
Marital status: single/unmarried	0.01	-1.2, 1.1	0.99
Prior surgery	0.2	-0.02, 0.4	0.08
PTSD	0.3	-0.3, 1.0	0.34
Race: Asian	0.5	-0.3, 1.3	0.26
Race: Black or African American	-0.3	-1.5, 0.9	0.58
Race: multi-racial	0.6	-0.1, 1.4	0.11
Race: Native American or Alaskan Native	0.1	-0.8, 1.1	0.81
Race: White	-0.2	-0.7, 0.2	0.31
Sleep apnea	0.1	-0.1, 0.3	0.41
Sleep insomnia	0.2	-0.1, 0.4	0.21
Nicotine dependence	0.1	-0.2, 0.4	0.55

Bold values indicate significant association. PTSD, post-traumatic stress disorder.

the OSPRO-YF scores by sex in this study identified possible differences in the negative coping domain but was not statistically significant ($p = 0.08$).

Our finding that female sex decreased the extent of pain-related psychological distress differs from reports in previous studies.⁶⁵ For example, female sex was associated with severe psychological distress in patients receiving orthopedic care for shoulder pain.⁶⁶ Our study controlled for surgical history, whereas the aforementioned study included patients undergoing rehabilitation and operative management. In this case, the differences in patient characteristics and intervention strategy may influence the generalizability of the results. Further investigation into sex-specific differences in the OSPRO-YF 10 negative coping items may reveal a protective association with yellow flag count.⁴⁵ Furthermore, analysis of items in the fear-avoidance and catastrophizing domains of the OSPRO-YF 17 would enhance the understanding of different responses between sexes.

Sensitivity analyses identified that previous surgical history (hip/knee arthroplasty or spine) influenced the OSPRO-YF 10 simple summary score, which to our knowledge, has not been investigated and may provide early evidence of an association between surgery and psychological distress. The variance in the association of the covariates may represent subtle differences in the scoring methods. In addition, some comorbidities were excluded from the models due to such few cases (i.e., PTSD in only five individuals).

Clinical implications

Understanding the associations of pain-related comorbidities with pain intensity, pain-related psychological distress, and other relevant outcomes remain important for the future of healthcare. Medical professionals often synthesize a long list of potentially relevant factors influencing pain outcomes. It has been estimated that 75–85% of depression goes untreated⁶⁷ and improving primary care providers'

screening of depression has increased the odds of subsequent diagnosis and treatment.⁶⁸ Additionally, physical therapists have identified that comorbid depression may be highly influential in patient management, but they only formally screen for it during 18% of physical therapy evaluations.^{22,69} Our study may help fill this knowledge gap for clinicians and inform subsequent psychologically informed management for pain-related outcomes.^{31,70} The results highlight the need to further explore multidisciplinary collaboration as a potential to influence the trajectory of pain and healthcare costs.^{5,71}

Limitations

There are limitations to this study. First, the results may lack generalizability in some settings as 95.3% of this sample was white with a median age of 59.0 years, and only individuals with spinal pain or hip/knee OA were included. Studies conducted with a larger diversity of race have demonstrated associations between pain-related comorbidities and pain intensity.³⁸ Some comorbidities affect different populations disproportionately,⁷² and these results should be validated in more diverse cohorts. Second, all data collected were from one health system, which may reduce generalizability. Third, the stage and severity of the MSP disorders and comorbidities were not available and their impact on outcomes may vary. Fourth, the differing results on the OSPRO-YF 10 analysis between total yellow flag count and the sensitivity analyses for simple summary score and yellow flag domain count scoring indicate the results should be interpreted with caution as the findings were not consistent across the three methods (thus our multiple sensitivity analyses). Consensus on the most appropriate interpretation of the OSPRO-YF 10 is still lacking.^{30,65} Fifth, no causal claims can be made about these relationships, and further validation using a design to assess prospective changes in pain is recommended for more definitive conclusions.

Conclusion

In our models, depression was the only comorbidity associated with greater pain intensity. None of the pain-related comorbidities were associated with pain-related psychological distress. Prior surgery in the primary area of care-seeking was associated with pain intensity. Lastly, female sex demonstrated a protective benefit for pain-related psychological distress which is worth further exploration. Clinicians working with patients with MSP conditions should consider the relationship between comorbid depression and other variables (such as the location of symptoms and a prior history of surgery), and pain intensity reported by the patient during the initial consultation.

Conflicts of interest

No authors have any competing or conflicts of interest to declare. This article represents the opinion of the authors and does not reflect any official position of the Uniformed Services University, Department of Defense, Department of Health and Human Services, U.S. Public Health Service or Indian Health Service, or United States Government.

Supplementary materials

Supplementary material associated with this article can be found in the online version at [doi:10.1016/j.bjpt.2023.100532](https://doi.org/10.1016/j.bjpt.2023.100532).

References

1. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ.* 2003;81(9):646–656.
2. Hurwitz EL, Randhawa K, Yu H, Côté P, Haldeman S. The Global Spine Care Initiative: a summary of the global burden of low back and neck pain studies. *Eur Spine J.* 2018;27(Suppl 6):796–801.
3. Ren K. Grand challenges in musculoskeletal pain research: chronicity, comorbidity, immune regulation, sex differences, diagnosis, and treatment opportunities. *Front Pain Res.* 2020;1. <https://doi.org/10.3389/fpain.2020.575479>.
4. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth.* 2019;123(2):e273–e283.
5. El-Tallawy SN, Nalamasu R, Salem GI, LeQuang JAK, Pergolizzi JV, Christo PJ. Management of musculoskeletal pain: an update with emphasis on chronic musculoskeletal pain. *Pain Ther.* 2021;10(1):181–209.
6. Rhon DI, Clewley D, Young JL, Sissel CD, Cook CE. Leveraging healthcare utilization to explore outcomes from musculoskeletal disorders: methodology for defining relevant variables from a health services data repository. *BMC Med Inform Decis Mak.* 2018;18(1):10.
7. Dahan A, van Velzen M, Niesters M. Comorbidities and the complexities of chronic pain. *Anesthesiology.* 2014;121(4):675–677.
8. Blyth FM, Briggs AM, Schneider CH, Hoy DG, March LM. The global burden of musculoskeletal pain-where to from here? *Am J Public Health.* 2019;109(1):35–40.
9. Young JL, Wright AA, Rhon DI. Nonoperative management prior to hip arthroscopy for femoroacetabular impingement syndrome: an investigation into the utilization and content of physical therapy. *J Orthop Sports Phys Ther.* 2019;49(8):593–600.
10. Roizenblatt S, Souza AL, Palombini L, Godoy LM, Tufik S, Bittencourt LRA. Musculoskeletal Pain as a Marker of Health Quality. Findings from the epidemiological sleep study among the adult population of São Paulo City. *PLoS One.* 2015;10(11):e0142726.
11. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. *J Pain.* 2011;12(9):964–973.
12. Husak AJ, Bair MJ. Chronic pain and sleep disturbances: a pragmatic review of their relationships, comorbidities, and treatments. *Pain Med.* 2020;21(6):1142–1152.
13. Dong HJ, Gerdle B, Bernfort L, Levin LÅ, Dragioti E. Pain catastrophizing in older adults with chronic pain: the mediator effect of mood using a path analysis approach. *J Clin Med Res.* 2020;9(7). <https://doi.org/10.3390/jcm9072073>.
14. VanDenKerkhof EG, Peters ML, Bruce J. Chronic pain after surgery: time for standardization? A framework to establish core risk factor and outcome domains for epidemiological studies. *Clin J Pain.* 2013;29(1):2–8.
15. Parkerson HA, Zvolensky MJ, Asmundson GJG. Understanding the relationship between smoking and pain. *Expert Rev Neurother.* 2013;13(12):1407–1414.
16. Clewley D, Rhon D, Flynn T, Koppenhaver S, Cook C. Health seeking behavior as a predictor of healthcare utilization in a population of patients with spinal pain. *PLoS One.* 2018;13(8):e0201348.
17. Grimby-Ekman A, Gerdle B, Björk J, Larsson B. Comorbidities, intensity, frequency and duration of pain, daily functioning and health care seeking in local, regional, and widespread pain - a descriptive population-based survey (SwePain). *BMC Musculoskelet Disord.* 2015;16(1):165.
18. Pain management best practices inter-agency task force. *Pain Management Best Practices Inter-Agency Task Force Report Updates, Gaps, Inconsistencies, and Recommendations.* U.S. Department Health & Human Services; 2019. <https://www.hhs.gov/sites/default/files/pmtf-final-report-2019-05-23.pdf>.
19. Lugtenberg M, Burgers JS, Clancy C, Westert GP, Schneider EC. Current guidelines have limited applicability to patients with comorbid conditions: a systematic analysis of evidence-based guidelines. *PLoS One.* 2011;6(10):e25987.
20. Nelson S, Simons LE, Logan D. The incidence of adverse childhood experiences (ACEs) and their association with pain-related and psychosocial impairment in youth with chronic pain. *Clin J Pain.* 2018;34(5):402–408.
21. Reme SE, Dennerlein JT, Hashimoto D, Sorensen G. Musculoskeletal pain and psychological distress in hospital patient care workers. *J Occup Rehabil.* 2012;22(4):503–510.
22. Young SB, Aprill C, Braswell J, Ogard WK, Richards JS, McCarthy JP. Psychological factors and domains of neck pain disability. *Pain Med.* 2009;10(2):310–318.
23. Archer KR, Wegener ST, Seebach C, et al. The effect of fear of movement beliefs on pain and disability after surgery for lumbar and cervical degenerative conditions. *Spine.* 2011;36(19):1554–1562.
24. Wahlman M, Häkkinen A, Dekker J, Marttinen I, Vihtonen K, Neva MH. The prevalence of depressive symptoms before and after surgery and its association with disability in patients undergoing lumbar spinal fusion. *Eur Spine J.* 2014;23(1):129–134.
25. Archer KR, Abraham CM, Obremskey WT. Psychosocial factors predict pain and physical health after lower extremity trauma. *Clin Orthop Relat Res.* 2015;473(11):3519–3526.
26. Pérez-Prieto D, Gil-González S, Pelfort X, Leal-Blanquet J, Puig-Verdié L, Hinarejos P. Influence of depression on total knee arthroplasty outcomes. *J Arthroplasty.* 2014;29(1):44–47.

27. Torres-Claramunt R, Hinarejos P, Amestoy J, et al. Depressed patients feel more pain in the short term after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(11):3411–3416.
28. Legha A, Burke DL, Foster NE, et al. Do comorbidities predict pain and function in knee osteoarthritis following an exercise intervention, and do they moderate the effect of exercise? Analyses of data from three randomized controlled trials. *Musculoskeletal Care.* 2019. <https://doi.org/10.1002/msc.1425>. Published online December 14.
29. George SZ, Beneciuk JM, Lentz TA, et al. Optimal Screening for Prediction of Referral and Outcome (OSPRO) for musculoskeletal pain conditions: results from the validation cohort. *J Orthop Sports Phys Ther.* 2018;48(6):460–475.
30. Horn ME, George SZ, Li C, Luo S, Lentz TA. Derivation of a risk assessment tool for prediction of long-term pain intensity reduction after physical Therapy. *J Pain Res.* 2021;14:1515–1524.
31. Lentz TA, George SZ, Beneciuk JM, et al. Development of a review-of-systems screening tool for orthopaedic physical therapists: results from the Optimal Screening for Prediction of Referral and Outcome (OSPRO) Cohort. *J Orthop Sports Phys Ther.* 2016;46(5):327–343.
32. Geschwind N, Meulders M, Peters ML, Vlaeyen JWS, Meulders A. Can experimentally induced positive affect attenuate generalization of fear of movement-related pain? *J Pain.* 2015;16(3):258–269.
33. Smith BW, Zautra AJ. Vulnerability and resilience in women with arthritis: test of a two-factor model. *J Consult Clin Psychol.* 2008;76(5):799–810.
34. Turner JA, Jensen MP, Warms CA, Cardenas DD. Catastrophizing is associated with pain intensity, psychological distress, and pain-related disability among individuals with chronic pain after spinal cord injury. *Pain.* 2002;98(1–2):127–134.
35. Larsson B, Dragioti E, Grimby-Ekman A, Gerde B, Björk J. Predictors of chronic pain intensity, spread, and sensitivity in the general population: a two-year follow-up study from the SWE-PAIN cohort. *J Rehabil Med.* 2019;51(3):183–192.
36. Mok LC, Lee IFK. Anxiety, depression and pain intensity in patients with low back pain who are admitted to acute care hospitals. *J Clin Nurs.* 2008;17(11):1471–1480.
37. Oliveira DS, Vêlia Ferreira Mendonça L, Sofia Monteiro Sampaio R, Manuel Pereira Dias de Castro-Lopes J, Ribeiro de Azevedo LF. The impact of anxiety and depression on the outcomes of chronic low back pain multidisciplinary pain management—a multicenter prospective cohort study in pain clinics with one-year follow-up. *Pain Med.* 2019;20(4):736–746.
38. Liu F, Fang T, Zhou F, et al. Association of depression/anxiety symptoms with neck pain: a systematic review and meta-analysis of literature in China. *Pain Res Manag.* 2018;2018: 3259431.
39. Benchimol EI, Smeeth L, Guttman A, et al. The reporting of studies conducted using observational routinely-collected health data (RECORD) statement. *Z Evid Fortbild Qual Gesundheitswes.* 2016;115–116. 33–48.
40. Lentz TA, Harman JS, Marlow NM, Beneciuk JM, Fillingim RB, George SZ. Factors associated with persistently high-cost health care utilization for musculoskeletal pain. *PLoS One.* 2019;14(11): e0225125.
41. Lentz TA, Beneciuk JM, George SZ. Prediction of healthcare utilization following an episode of physical therapy for musculoskeletal pain. *BMC Health Serv Res.* 2018;18(1):648.
42. Bernstein DN, Kelly M, Houck JR, et al. PROMIS pain interference is superior vs numeric pain rating scale for pain assessment in foot and ankle patients. *Foot Ankle Int.* 2019;40(2):139–144.
43. Young IA, Dunning J, Butts R, Cleland JA, Fernández-de-Las-Peñas C. Psychometric properties of the Numeric Pain Rating Scale and Neck Disability Index in patients with cervicogenic headache. *Cephalalgia.* 2019;39(1):44–51.
44. Jensen MP, Karoly P, O’Riordan EF, Bland Jr F, Burns RS. The subjective experience of acute pain. An assessment of the utility of 10 indices. *Clin J Pain.* 1989;5(2):153–159.
45. Butera KA, George SZ, Lentz TA. Psychometric evaluation of the optimal screening for prediction of referral and outcome yellow flag (OSPRO-YF) tool: factor structure, reliability, and validity. *J Pain.* 2019. <https://doi.org/10.1016/j.jpain.2019.09.003>. Published online September 18.
46. Underwood MR, Harding G, Klaber Moffett J, UK BEAM trial team. Patient perceptions of physical therapy within a trial for back pain treatments (UK BEAM) [ISRCTN32683578]. *Rheumatology.* 2006;45(6):751–756.
47. Stearns ZR, Carvalho ML, Beneciuk JM, Lentz TA. Screening for yellow flags in orthopaedic physical therapy: a clinical framework. *J Orthop Sports Phys Ther.* 2021;51(9):459–469.
48. Kenne Pagui EC, Salvan A, Sartori N. Improved estimation in negative binomial regression. *Stat Med.* 2022;41(13):2403–2416.
49. Goulet JL, Buta E, Bathulapalli H, Gueorguieva R, Brandt CA. Statistical models for the analysis of zero-inflated pain intensity numeric rating scale data. *J Pain.* 2017;18(3):340–348.
50. Rhon DI, Snodgrass SJ, Cleland JA, Greenlee TA, Sissel CD, Cook CE. Comparison of downstream health care utilization, costs, and long-term opioid use: physical therapist management versus opioid therapy management after arthroscopic hip surgery. *Phys Ther.* 2018;348(5).
51. Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic factors for pain chronicity in low back pain: a systematic review. *Pain Rep.* 2021;6(1):e919.
52. Zheng S, Tu L, Cicuttini F, et al. Depression in patients with knee osteoarthritis: risk factors and associations with joint symptoms. *BMC Musculoskelet Disord.* 2021;22(1):40.
53. Roughan WH, Campos AI, Garcia-Marin LM, et al. Comorbid chronic pain and depression: shared risk factors and differential antidepressant effectiveness. *Front Psychiatry.* 2021;12: 643609.
54. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. *Clin J Pain.* 1997;13(2):116–137.
55. Bondesson E, Larrosa Pardo F, Stigmar K, et al. Comorbidity between pain and mental illness - evidence of a bidirectional relationship. *Eur J Pain.* 2018;22(7):1304–1311.
56. Walsh TP, Arnold JB, Evans AM, Yaxley A, Damarell RA, Shanahan EM. The association between body fat and musculoskeletal pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord.* 2018;19(1):233.
57. Peiris WL, Cicuttini FM, Hussain SM, et al. Is adiposity associated with back and lower limb pain? A systematic review. *PLoS One.* 2021;16(9): e0256720.
58. Lentz TA, George SZ, Manickas-Hill O, et al. What general and pain-associated psychological distress phenotypes exist among patients with hip and knee osteoarthritis? *Clin Orthop Relat Res.* 2020;478(12):2768–2783.
59. Skogö Nyvang J, Naili JE, Iversen MD, Broström EW, Hedström M. Younger age is associated with greater pain expression among patients with knee or hip osteoarthritis scheduled for a joint arthroplasty. *BMC Musculoskelet Disord.* 2019;20(1):365.
60. Staud R, Price DD, Robinson ME, Vierck Jr. CJ. Body pain area and pain-related negative affect predict clinical pain intensity in patients with fibromyalgia. *J Pain.* 2004;5(6):338–343.
61. Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D. Localized or widespread musculoskeletal pain: does it matter? *Pain.* 2008;138(1):41–46.
62. Bruce J, Quinlan J. Chronic post surgical pain. *Rev Pain.* 2011;5(3):23–29.
63. Reuben SS. Chronic pain after surgery: what can we do to prevent it? *Curr Pain Headache Rep.* 2007;11(1):5–13.
64. Poleshuck EL, Katz J, Andrus CH, et al. Risk factors for chronic pain following breast cancer surgery: a prospective study. *J Pain.* 2006;7(9):626–634.

65. George SZ, Li C, Luo S, Horn ME, Lentz TA. Longitudinal monitoring of pain associated distress with the optimal screening for prediction of referral and outcome yellow flag tool: predicting reduction in pain intensity and disability. *Arch Phys Med Rehabil.* 2020;101(10):1763–1770.
66. Levin JM, Baker R, Goltz D, et al. Heterogeneity of pain-related psychological distress in patients seeking care for shoulder pathology. *J Shoulder Elbow Surg.* 2021. <https://doi.org/10.1016/j.jse.2021.09.009>. Published online October 14.
67. Mitchell AJ, Vaze A, Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. *Lancet.* 2009;374(9690):609–619.
68. Samples H, Stuart EA, Saloner B, Barry CL, Mojtabai R. The role of screening in depression diagnosis and treatment in a representative sample of US primary care visits. *J Gen Intern Med.* 2020;35(1):12–20.
69. Fay P, Edmond SL, Baron JK, Joshi M. Depression screening by physical therapists: practices, beliefs, barriers. *J Back Musculoskelet Rehabil.* 2017;30(6):1221–1229.
70. Nicholas MK, Linton SJ, Watson PJ, Main CJ. Early identification and management of psychological risk factors (“yellow flags”) in patients with low back pain: a reappraisal. *Phys Ther.* 2011;91(5):737–753.
71. Lentz TA, Hellkamp AS, Bhavsar NA, Goode AP, Manhapra A, George SZ. Assessment of common comorbidity phenotypes among older adults with knee osteoarthritis to inform integrated care models. *Mayo Clin Proc Innov Qual Outcomes.* 2021;5(2):253–264.
72. Kalgotra P, Sharda R, Croff JM. Examining multimorbidity differences across racial groups: a network analysis of electronic medical records. *Sci Rep.* 2020;10(1):13538.