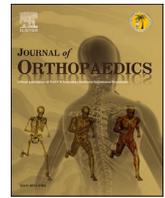




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Predictors of postoperative pain using PROMIS pain interference two-years following knee surgery

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ABSTRACT

Introduction: The purpose of this study was to identify preoperative factors associated with worse PROMIS Pain Interference (PI) two years following knee surgery.

Methods: Participants completed surveys preoperatively and two years postoperatively. Data collected included demographics, medical history, and multiple patient-reported outcomes measures, including PROMIS PI.

Results: After controlling for confounders, lower income, smoking, worse PROMIS Anxiety, worse Numeric Pain Score body pain, and worse Marx Activity Rating Scale were independent predictors for worse PROMIS PI two years after surgery.

Conclusion: Worse PROMIS PI two years after elective knee surgery is associated with multiple socio-demographic patient identifiers.

1. Introduction

Postoperative pain management is a critical issue in the context of the ongoing opioid epidemic, especially for orthopaedic surgeons who have been previously cited as the third highest prescribers.^{1,2} As the number of orthopaedic knee surgeries performed continues to rise each year,^{3–5} it is important to develop an understanding of what factors may influence postoperative pain.⁶ To evaluate treatment effectiveness, researchers and clinicians need psychometrically sound and clinically valid instruments for measuring different aspects of pain. Identifying modifiable and nonmodifiable factors associated with postoperative pain may help orthopaedic surgeons develop targeted strategies for postoperative pain management and decrease the overall need for opioids.

Pain is a multidimensional construct, and previous studies have shown that postoperative pain may be influenced by various factors such as preoperative pain, age, depression, anxiety, or chronicity.^{7–9} These findings emphasize the importance of psychometric patient characteristics and underscores the need for comprehensive health assessment, including multiple facets of a patients' health status. An important

aspect of pain is 'pain interference' – the degree to which pain interferes with an individual's daily activities and is viewed as an important assessment of the patient pain experience.

The National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS)¹⁰ is a family of instruments that can be used to measure different aspects of physical, mental, and social health, including Pain Interference (PI).^{11,12} The psychometric properties of the PROMIS PI measure have been previously evaluated in a large cross-sectional sample of patients undergoing knee surgery,¹³ however, longitudinal data is lacking.

The PROMIS measures have been shown to be comparable to traditional assessments or legacy PROs in multiple areas of medicine,^{14–17} but the clinical validity of the scores in a wide variety of orthopedic contexts has yet to be established. The objective of this study was to identify preoperative factors associated with worse PROMIS PI two-years following knee surgery. We hypothesized that worse preoperative pain, preoperative physical function, and psychosocial factors would be associated with worse two-year and improvement PROMIS PI scores two-years after elective knee surgery.

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2. Methods

Patients undergoing orthopaedic knee surgery at a single urban academic institution were evaluated preoperatively from August 2015 to March 2017. Inclusion criteria were as follows: (1) patients undergoing knee surgery, (2) age 17 years and older, (3) English-speaking, and (4) able to provide consent. Exclusion criteria included: (1) inability to speak or read English, (2) incarcerated, and (3) wards of the state. Eligible patients were approached by research staff for enrollment into an Institutional Review Board (IRB)-approved, prospective web-based registry.¹⁸ Survey data was collected preoperatively and at two-years postoperatively, and managed using Research Electronic Data Capture (REDCap™).^{19,20}

A total of 490 registry participants completed preoperative surveys regarding demographics, general health, pain, function, activity level, and expectations. Electronic medical records were used to record other patient factors such as Common Procedural Terminology (CPT) code, American Society of Anesthesiologists (ASA) score, surgical history, comorbidities, and preoperative opioid use. CPT codes were confirmed by reviewing the operative note, and they were analyzed both by primary code and by all codes combined to account for multiple procedural codes. All patients were administered questionnaires from six domains of the PROMIS Computer Adaptive Testing (CAT) domains, including PI, Physical Function (PF), Social Satisfaction (SS), Fatigue, Anxiety, and Depression. All PROMIS measures were administered utilizing CAT and question banks. The use of item banks allows for more flexible administration using CAT, a tailored approach in which the questions administered are selected based on individuals' responses to previous items.

The PROMIS PI measure item-bank is calibrated using the graded response model that estimates item location (severity) and discrimination (ability to distinguish among people with different levels of the pain outcome). Furthermore, PROMIS PI is scored on an inverted scale where higher numeric value indicates higher pain interference. To minimize confusion, we describe PROMIS PI scores as "better" (lower PROMIS PI score) or "worse" (higher PROMIS PI score) throughout the manuscript.

Traditional PRO measures were also collected for comparison. The Numeric Pain Scale (NPS) was used to assess operative knee (NPS knee) and whole body (NPS body) pain. Activity levels and function were assessed with the Tegner Activity Scale (TAS),²¹ Marx Activity Rating Scale (MARS),²² and International Physical Activity Questionnaire (IPAQ).²³ IPAQ scores were reported as Metabolic Equivalent Task minutes per week (MET-min/wk). Knee-specific outcomes were measured with the International Knee Documentation Committee (IKDC) subjective knee evaluation form.²⁴ Expectations of surgery were assessed with the Musculoskeletal Outcomes Data Evaluation and Management System (MODEMS) questionnaire.²⁵

2.1. Statistical analysis

PROMIS PI and other PRO measures were administered at baseline and at two-year follow-up. Continuous data was reported as means and standard deviations, while categorical data was reported as frequencies and percentages. Change from baseline scores were calculated for each PRO measure by subtracting the baseline score from the two-year score. For inverted scales like PROMIS PI, negative numbers indicate improvement, and the greater the improvement from baseline, the greater the negative number. Kruskal-Wallis and Wilcoxon rank-sum tests were used for comparison of means among more than two groups or between two groups, respectively. For comparisons of more than two means, post-hoc Wilcoxon rank-sum was performed. Spearman rank correlation coefficient (ρ_s) was used to determine the correlation between continuous variables such as PROs and PROMIS PI. Backwards stepwise multivariable regression was performed to determine preoperative predictors for final and change in two-year PROMIS PI scores. All statistical tests were two-sided and the *P*-value for significance was set at

P < 0.05. The analyses were performed using JMP Pro, Version 13 software (JMP®, Version 13. SAS Institute Inc., Cary, North Carolina).

3. Results

Four hundred ninety patients completed the preoperative surveys, of which 359 patients (73.3%) completed two-year follow-up. The mean PROMIS PI significantly improved from 60.5 to 51.1 (Table 1, *p* < 0.001). The ten most frequent primary and all CPT codes are shown in Tables 2 and 3, respectively. The analysis showed similar results for both primary CPT and all CPT codes, with significantly better two-year PROMIS PI for anterior cruciate ligament reconstruction (29888) and meniscus repair (29882) and significantly worse PROMIS PI for total knee arthroplasty (27447).

Bivariate analysis demonstrated multiple preoperative categorical variables to be associated with worse two-year PROMIS PI scores (Table 4). Socio-demographic factors associated with worse two-year PI included: female gender, Black race, non-Hispanic/Latino ethnicity, income less than \$70k, government-sponsored insurance, high school graduate as highest level of education, unemployment, associated legal claim, and being single. Clinical factors associated with worse two-year PI included: history of smoking, history of depression or anxiety, history of preoperative opioid use, and no history of injury prior to surgery. Concerning surgical factors, arthroplasty and non-arthroscopic procedures were also associated with worse two-year PI.

For preoperative continuous variables, older age, higher BMI, greater number of comorbidities, and greater number of previous surgeries were all associated with worse two-year PROMIS PI (Table 5). Older age, greater number of comorbidities, greater number of previous surgeries, lower expectations, non-Hispanic/Latino ethnicity, smoking, and a legal claim were associated with less improvement in PROMIS PI (Table 5).

Better preoperative scores on all preoperative patient-reported outcome measures were correlated with better two-year PROMIS PI (Table 6). Less improvement in PROMIS PI was correlated with better preoperative PROMIS PI, higher MARS, and lower PROMIS Physical Function (Table 6).

After controlling for confounding variables, multivariable analysis demonstrated that income, smoking, PROMIS Anxiety, NPS Body, and MARS scores were independent predictors of two-year PROMIS PI, accounting for 38% of the variance in the two-year PROMIS PI scores (Table 7). More specifically, income less than \$70k, higher PROMIS Anxiety, and higher NPS Body scores were predictors of worse two-year PROMIS PI scores while never-smoker status and higher MARS were predictors of better two-year PI. The independent predictors of change in PROMIS PI were similar to those of final two-year PROMIS PI and accounted for 33% of the variance (Table 8). In this model, less improvement in PROMIS PI was independently predicted by income less than \$70k, higher PROMIS Anxiety, higher NPS body scores, lower MARS scores, and better preoperative PROMIS PI.

4. Discussion

The findings of this study support the hypothesis that worse preoperative pain and psychosocial factors are predictors of worse postoperative pain interference and worse improvement in postoperative

Table 1
PROMIS pain interference scores.

	Preoperative		Postoperative		Change		P-value
	Mean	SD	Mean	SD	Mean	SD	
PROMIS Pain Interference	60.5	7.2	51.1	9.9	-9.1	9.5	<.001

Kruskal-Wallis Test was used for comparison of means among two groups. *P* value for significance was set at *P* < 0.05. Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; SD, Standard Deviation.

Table 2
Top ten primary common procedural terminology (CPT) codes by two-year PROMIS pain interference (PI).

CPT Code	Description	Count	PROMIS PI (SD) ^a	P-value ^b
29888	Arthroscopically aided anterior cruciate ligament repair/ augmentation or reconstruction	88	47.8 (9.3)	<0.001
29881	Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving)	57	51.1 (10.4)	0.96
27447	Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing (total knee arthroplasty)	33	57.3 (10.7)	<0.001
29870	Arthroscopy, knee, diagnostic, with or without synovial biopsy (separate procedure)	30	50.0 (9.8)	0.53
29879	Arthroscopy, knee, surgical; abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture	28	54.2 (9.6)	0.67
29882	Arthroscopy, knee, surgical; with meniscus repair (medial OR lateral)	22	47.2 (7.4)	0.042
29876	Arthroscopy, knee, surgical; synovectomy, major, 2 or more compartments (eg, medial or lateral)	22	50.0 (11.4)	0.54
27446	Arthroplasty, knee, condyle and plateau; medial OR lateral compartment	18	52.9 (7.7)	0.31
29877	Arthroscopy, knee, surgical; debridement/shaving of articular cartilage (chondroplasty)	10	55.0 (11.2)	0.21
29880	Arthroscopy, knee, surgical; with meniscectomy (medial AND lateral, including any meniscal shaving)	6	56.4 (9.6)	0.24

^a Mean two-year PI was compared using Wilcoxon/Kruskal-Wallis Tests. P value for significance was set at P < 0.05. There was a statistically significant difference between primary CPT codes (P < 0.001).

^b Individual CPT PI scores were analyzed post-hoc using Wilcoxon Rank-Sum Test. Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; SD, Standard Deviation.

pain interference two-years after knee surgery. Preoperative knee function was not an independent predictor of PROMIS PI, but activity level as measured by MARS was an independent predictor. The recent increase in the utilization of PROMIS outcome measures in orthopaedic surgery have demonstrated their validity and reliability when compared to legacy measures.^{13,26–29} Specifically, PROMIS PI has been shown to be a potentially more clinically relevant PRO than NPS as it characterizes the degree to which pain limits or interferes with individuals' physical, mental, and social activities.^{13,30} To the best of our knowledge, this is the first study to evaluate and identify predictors of PROMIS PI of two years postoperatively in patients undergoing elective knee surgery. Identifying those patients at higher risk of postoperative pain may allow for modification of treatment.^{31,32}

One of the main findings of our study was the identification of psychosocial factors as a predictor of postoperative pain. Specifically, psychological differences between patients may be an important contributing factor to the mismatch between postoperative knee function scores and rates of return to activity.³³ The different psychological and behavioral responses to pain amongst patients are some of the most well-researched factors that may contribute to a lack of return to activity following knee surgery.^{33–37} Specifically, we found anxiety and low-income to be significant predictors of worse postoperative PROMIS PI and worse improvement in PROMIS PI. It has been previously hypothesized that stress and depression globally affect physical and mental health, and that a person's degree of socioeconomic support modulate this effect.³⁸ The relationship between anxiety (i.e. stress), depression, and pain may strongly influence symptom severity and the ability to

Table 3
Top ten All common procedural terminology (CPT) codes.

CPT Code	Description	Count	Two Year PROMIS PI (SD) ^a	P-value ^b
29881	Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving)	118	51.2 (10.6)	0.91
29888	Arthroscopically aided anterior cruciate ligament repair/ augmentation or reconstruction	105	48.2 (9.3)	<0.001
29876	Arthroscopy, knee, surgical; synovectomy, major, 2 or more compartments	78	49.5 (9.8)	0.11
29879	Arthroscopy, knee, surgical; abrasion arthroplasty or multiple drilling or microfracture	61	51.5 (10.0)	0.71
29882	Arthroscopy, knee, surgical; with meniscus repair (medial OR lateral)	61	48.0 (8.8)	<0.001
29877	Arthroscopy, knee, surgical; debridement/shaving of articular cartilage (chondroplasty)	43	50.7 (9.5)	0.84
27447	Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing (total knee arthroplasty)	36	57.1 (10.5)	<0.001
27446	Arthroplasty, knee, condyle and plateau; medial OR lateral compartment	21	54.3 (6.8)	0.07
29874	Arthroscopy, knee, surgical; for removal of loose body or foreign body (eg, osteochondritis dissecans fragmentation, chondral fragmentation)	19	48.8 (8.4)	0.34
27427	Ligamentous reconstruction (augmentation), knee; extra-articular	17	49.4 (9.3)	0.62

^a Mean two-year PI was compared using Wilcoxon/Kruskal-Wallis Tests. P value for significance was set at P < 0.05. There was a statistically significant difference between primary CPT codes (P < 0.001).

^b Individual CPT PI scores were analyzed post hoc using Wilcoxon Rank-Sum Test. Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System; SD, Standard Deviation.

recover from surgery in patients with musculoskeletal conditions, though the relationship is not entirely clear based on current studies. A prospective study by Hirschmann et al. reported that preoperative and postoperative anxiety scores both significantly correlated with worse knee pain scores preoperatively and at one-year follow-up.³⁹ Lavernia et al. found that distressed patients had lower postoperative pain scores at a minimum two-year follow-up; however, the magnitude of improvement in pain was similar between distressed and nondistressed patients.⁴⁰ Blackburn et al. found that patients with postoperative improvements in anxiety and depression also had greater improvements in pain scores, suggesting that the pain relief afforded by surgery could help improve mental health.⁴¹

A few studies have demonstrated that worse preoperative PROMIS PI scores are associated with better postoperative score improvement.^{42–44} Chen et al. reported that patients with preoperative PROMIS PI scores of greater than 56.2 were more likely to achieve a minimal clinically important difference in improvement of score after primary anterior cruciate ligament reconstruction.⁴² Similarly, Ho et al. and Bernstein et al. found that patients with preoperative PROMIS PI scores greater than 67 and 68.2 were more likely to have clinically significant postoperative score improvement after foot-and-ankle and hand surgery, respectively.^{43,44} Our findings support this, demonstrating that worse preoperative PROMIS PI was a predictor of better improvement in two-year postoperative PROMIS PI. A patient with a better preoperative PROMIS PI score has less room for improvement since their pain was not

Table 4
PROMIS pain interference (PI) across categorical variables.

	Two-Year PI			Change PI		
	N (%)	Mean (SD)	P-value	N (%)	Mean (SD)	P-value
Gender						
Male	199 (55)	50.0 (9.8)	.01	196 (55)	-9.6 (9.5)	.24
Female	160 (45)	52.5 (9.9)		158 (45)	-8.5 (9.5)	
Race						
Black	105 (31)	53.1 (1.9)	.045	102 (30)	-8.9 (2.0)	.63
White	202 (59)	50.6 (9.5)		200 (60)	-8.9 (8.7)	
Other	33 (10)	49.1 (7.8)		33 (10)	-1.4 (9.5)	
Ethnicity						
Non-Hispanic or Latino	332 (95)	51.2 (9.8)	.02	328 (95)	-8.8 (9.4)	.03
Hispanic or Latino	17 (5)	45.5 (1.1)		17 (5)	-13.7 (9.9)	
Education						
College Graduate	155 (47)	50.2 (8.7)	.007	155 (48)	-9.0 (9.0)	.55
Did not complete high school	29 (9)	48.5 (1.7)		29 (9)	-1.3 (1.5)	
High School Graduate	144 (44)	53.1 (1.6)		141 (43)	-8.6 (9.8)	
Employment status						
Currently Employed	195 (59)	51.2 (9.1)	<.001	193 (59)	-8.7 (9.3)	.01
Student	64 (19)	45.9 (8.7)		64 (19)	-11.3 (9.8)	
Not Currently Employed/Other	72 (22)	56.3 (1.2)		71 (22)	-7.2 (9.1)	
Marital Status						
Married or domestic partnership	140 (42)	52.7 (8.9)	.02	140 (43)	-8.7 (8.8)	.54
Single/Other	192 (58)	50.3 (1.4)		189 (57)	-9.1 (9.9)	
Caregiver Status						
Available	291 (89)	51.1 (9.7)	.63	288 (89)	-9.2 (9.4)	.17
Not Available	36 (11)	52.0 (1.6)		36 (11)	-6.8 (8.9)	
Family/Friend Caregiver Status						
Family/Friend Available	321 (98)	51.1 (9.8)	.92	318 (98)	-9.0 (9.5)	.85
Family/Friend Not Available	8 (2)	51.1 (9.0)		8 (2)	-7.9 (9.0)	
Income						
< \$70,000	97 (45)	53.6 (1.9)	<.001	97 (45)	-8.3 (1.2)	.09
≥ \$70,000	120 (55)	48.4 (8.1)		120 (55)	-1.6 (8.8)	
Insurance Status						
Private Insurance	283 (81)	50.1 (9.5)	.001	281 (81)	-9.5 (9.5)	.27
Government Sponsored	67 (19)	54.6 (11.1)		64 (19)	-8.0 (9.3)	
Smoking Status						
Smoker	26 (8)	60.7 (9.9)	<.001	25 (8)	-3.6 (9.2)	.005
Never smoked	244 (74)	50.1 (9.6)		243 (74)	-9.3 (9.3)	
Quit Smoking	61 (18)	52.0 (8.4)		60 (18)	-9.6 (9.6)	
Alcohol Consumption						
Never	91 (28)	50.6 (1.7)	.07	90 (28)	-1.4 (1.4)	0.15
4 times per month or fewer	160 (49)	52.4 (9.6)		158 (48)	-7.9 (9.1)	
Greater than 4 times per month	77 (23)	49.8 (9.1)		77 (24)	-9.3 (9.0)	
Recreational Drug Use						

Table 4 (continued)

	Two-Year PI			Change PI		
	N (%)	Mean (SD)	P-value	N (%)	Mean (SD)	P-value
No	309 (94)	51.5 (9.9)	.16	307 (94)	-8.8 (9.5)	.46
Yes	20 (6)	48.3 (7.8)		19 (6)	-1.3 (8.6)	
Marijuana Use						
No	311 (95)	51.4 (10.0)	.30	308 (94)	-8.8 (9.4)	.52
Yes	18 (5)	48.9 (7.8)		18 (6)	-1.1 (8.8)	
Preoperative Opioid Use						
No	288 (81)	50.0 (9.6)	<.001	283 (81)	-9.3 (9.7)	.46
Yes	68 (19)	56.4 (9.5)		68 (19)	-8.1 (8.7)	
IPAQ						
Low	111 (34)	53.9 (1.0)	.002	109 (34)	-9.5 (9.2)	.86
Moderate	86 (27)	50.1 (1.2)		86 (27)	-9.2 (1.2)	
High	128 (39)	49.8 (8.9)		127 (39)	-8.6 (9.0)	
Depression or Anxiety Diagnosis						
No	319 (89)	50.7 (9.9)	.01	314 (89)	-9.1 (9.7)	.77
Yes	39 (11)	54.6 (1.1)		39 (11)	-8.6 (8.2)	
Diabetes						
No	329 (92)	50.9 (9.9)	.07	325 (92)	-9.1 (9.6)	.76
Yes	28 (8)	54.1 (1.1)		27 (8)	-8.9 (9.6)	
Back Pain						
No	347 (98)	50.9 (9.9)	.02	344 (98)	-9.1 (9.6)	.86
Yes	6 (2)	60.0 (6.4)		6 (2)	-9.4 (4.7)	
Workers' Compensation						
No	7 (35)	55.0 (13.5)	.55	6 (32)	-9.5 (14.9)	.36
Yes	13 (65)	58.8 (1.0)		13 (68)	-3.0 (5.5)	
Legal Claim						
No	302 (93)	50.6 (9.7)	<.001	301 (94)	-9.3 (9.4)	.007
Yes	22 (7)	59.1 (10.0)		20 (6)	-3.9 (9.1)	
Laterality						
Left	175 (49)	50.6 (9.2)	.60	172 (49)	-8.8 (9.1)	.64
Right	183 (51)	51.6 (1.6)		181 (51)	-9.3 (9.9)	
Prior Surgery on Operative Joint						
No	226 (64)	50.7 (1.2)	.34	222 (64)	-9.4 (9.9)	.47
Yes	127 (36)	51.7 (9.5)		126 (36)	-8.5 (8.9)	
Injury Prior to Surgery						
No	121 (37)	53.9 (9.5)	<.001	120 (37)	-8.2 (8.9)	.24
Yes	206 (63)	49.7 (9.7)		204 (63)	-9.4 (9.6)	
ASA Score						
1	144 (40)	46.9 (8.6)	<.001	142 (40)	-1.4 (9.6)	.07
2	197 (55)	53.8 (9.9)		194 (55)	-8.3 (9.4)	
3	17 (5)	56.5 (8.3)		17 (5)	-7.5 (9.7)	
Arthroscopy						
No	87 (24)	53.7 (9.6)	.006	86 (24)	-9.1 (9.3)	.77
Yes	272 (76)	50.3 (9.9)		268 (76)	-9.1 (9.6)	

(continued on next page)

Table 4 (continued)

	Two-Year PI			Change PI		
	N (%)	Mean (SD)	P-value	N (%)	Mean (SD)	P-value
Arthroplasty						
No	306 (85)	50.3 (9.7)	<.001	302 (85)	-9.2 (9.6)	.76
Yes	53 (15)	55.7 (9.8)		52 (15)	-8.4 (9.1)	
Fracture						
No	359 (100)	51.1 (9.9)	NA	354 (100)	-9.1 (9.5)	NA
Yes	0 (0)	NA		0 (0)	NA	

Kruskal-Wallis and Wilcoxon rank-sum test were used for comparison of means among two or more groups. P value for significant was set at $P < 0.05$. *Abbreviations:* SD: standard deviation; PROMIS: Patient-Reported Outcome Measurement Information System; IPAQ: International Physical Activity Questionnaire; ASA: American Society of Anesthesiologists.

Table 5
PROMIS pain interference (PI) and continuous variable correlations.

Variable	Mean (SD)	Two-year PI		Change PI	
		r_s	P-value	r_s	P-value
Age	39.0 (16.3)	.33	<.001	.14	.007
Body Mass Index	29.4 (6.1)	.28	<.001	.03	.60
Number Comorbidities	0.5 (0.9)	.34	<.001	.13	.01
Number Prior Orthopaedic Surgeries	2.7 (3.2)	.07	.16	.03	.59
Number Prior Surgeries (Any)	1.6 (0.6)	.26	<.001	.13	.01
MODEMS Expectations	86.8 (17.1)	-.07	.18	-.15	.007

P value for significance was set at $P < 0.05$. *Abbreviations:* r_s (rho): Spearman's Rank Correlation Coefficient; PROMIS: Patient-Reported Outcome Measure Information Systems; SD, Standard Deviation; MODEMS: Musculoskeletal Outcomes Data Evaluation and Management System.

Table 6
Baseline PRO correlations with PROMIS pain interference (PI).

Baseline PROs	PROMIS PI	Two-year PI		Change PI	
		r_s	P-value	r_s	P-value
	PROMIS PF	-.30	<.001	-.29	<.001
	PROMIS Fatigue	.40	<.001	-.04	.51
	PROMIS SS	-.29	<.001	.01	.92
	PROMIS Anxiety	.32	<.001	.01	.92
	PROMIS Depression	.22	<.001	.03	.52
	IKDC	-.42	<.001	.09	.11
	NPS Knee	.31	<.001	-.07	.18
	NPS Body	.35	<.001	.09	.09
	IPAQ (METS-min/week)	-.11	.04	.06	.25
	TAS Pre-Injury	-.23	<.001	-.07	.22
	TAS Preoperative	-.30	<.001	.05	.39
	MARS	-.35	<.001	-.18	.002

P value for significance was set at $P < 0.05$. *Abbreviations:* r_s (rho): Spearman's Rank Correlation Coefficient; PROMIS: Patient-Reported Outcome Measure Information Systems; PF: Physical Function; SS: Social Satisfaction; IKDC: International Knee Documentation Committee; NPS: Numeric Pain Scale; IPAQ, International Physical Activity Questionnaire; MET: metabolic equivalents; TAS, Tegner Activity Scale; MARS: Marx Activity Rating Scale.

significantly affecting their day-to-day activities to begin with.

The adverse effects of smoking on healing after knee surgery has been well established.^{45–48} Our study demonstrates that smoking leads

Table 7

Multivariate linear regression model for two-year PROMIS pain interference (PI).

Two-year PROMIS PI	Term	Estimate	Standard Error	P-value	R ²
	Income Less than 70k	1.55	0.56	.006	.38
	Smoking (Never smoker)	-2.83	1.19	.018	
	PROMIS Anxiety	0.27	0.06	<.001	
	NPS Body	0.98	0.25	<.001	
	MARS	-0.07	0.01	<.001	

P value for significance was set at $P < 0.05$. Preoperative variables included in the stepwise backwards linear regression: Age, BMI, Number Prior Surgeries (Any), Number Comorbidities, Gender, Race, Ethnicity, Education, Marital status, Employment, Income, Insurance, Smoking, Preoperative Opioid Use, IPAQ, History of Depression or Anxiety, History of Back Pain, Injury Prior to Surgery, Procedure, ASA score, Legal Claim, IKDC, NPS Operative Joint, NPS Body, Tegner Preinjury, Tegner Current, Marx ARS, PROMIS PF, PROMIS Fatigue, PROMIS Anxiety, PROMIS Social Satisfaction, and PROMIS Depression. *Abbreviations:* PROMIS: Patient-Reported Outcome Measure Information Systems; BMI, Body Mass Index; NPS, Numeric Pain Scale; IPAQ, International Physical Activity Questionnaire; ASA, American Society of Anesthesiology; PF: Physical Function; SS: Social Satisfaction; IKDC: International Knee Documentation Committee; MARS: Marx Activity Rating Scale.

Table 8

Multivariate linear regression model for change in PROMIS pain interference (PI).

Two-year Change PROMIS PI	Term	Estimate	Standard Error	P-value	R ²
	Income Less than 70k	1.59	0.56	.005	.33
	PROMIS PI	-0.87	0.09	<.001	
	PROMIS Anxiety	0.24	0.07	<.001	
	NPS Body	0.86	0.27	.002	
	MARS	-0.07	0.02	<.001	

P value for significance was set at $P < 0.05$. Preoperative variables included in the stepwise backwards linear regression: Age, BMI, Number Prior Surgeries (Any), Number Comorbidities, Gender, Race, Ethnicity, Education, Marital status, Employment, Income, Insurance, Smoking, Preoperative Opioid Use, IPAQ, History of Depression or Anxiety, History of Back Pain, Injury Prior to Surgery, Procedure, ASA score, Legal Claim, IKDC, NPS Operative Joint, NPS Body, Tegner Preinjury, Tegner Current, Marx ARS, PROMIS PF, PROMIS Fatigue, PROMIS Anxiety, PROMIS Social Satisfaction, and PROMIS Depression. *Abbreviations:* PROMIS: Patient-Reported Outcome Measure Information Systems; BMI, Body Mass Index; NPS, Numeric Pain Scale; IPAQ, International Physical Activity Questionnaire; ASA, American Society of Anesthesiology; PF: Physical Function; SS: Social Satisfaction; IKDC: International Knee Documentation Committee; MARS: Marx Activity Rating Scale.

to poorer outcomes in terms of postoperative pain. Smokers had a significantly worse two-year postoperative PROMIS PI score, and a worse improvement in their PROMIS PI score from baseline. Jaiswal et al. combining arthroscopic findings and cartilage biopsies, demonstrated that even at one-year follow-up, the repair tissue in smokers who underwent knee surgery was inferior.⁴⁹ The authors also noted this smoking-based difference clinically in the modified Cincinnati score.⁴⁹ Current literature and our findings emphasize the negative influence of smoking on outcomes following knee surgery, and advocate for tobacco cessation counseling in all patients.

Of the physical function measures, PROMIS PF and Marx Activity Rating Scale (MARS) were the only functional measures which significantly correlated with both the two-year PROMIS PI score and change from baseline PI. However, MARS was the only significant predictor, demonstrating that patients with higher preoperative MARS score had a better two-year PROMIS PI score and a better improvement in their PROMIS PI score from baseline. Interestingly, Hancock et al.

demonstrated that MARS exhibited the weakest correlation with PROMIS PF, a relation most likely resulting from differences in instrument design and domain of assessment.⁵⁰ MARS consists of four questions assessing activity level based on the frequency of sport-related activities (i.e. cutting or pivoting), and has been advocated as a useful tool to evaluate post-rehabilitation progress in particularly active patients.^{22,51}

The potential modifying effect of age when interpreting surgical outcomes must be noted. Although increasing age was significantly correlated worse two-year PROMIS PI and change from baseline, it was not found to be significant predictor in our regression model, contrary to other studies.^{1,2,42} This is likely because our study population contained multiple age groups, with patients undergoing varying procedures, whereas other studies in the literature assessed only one specific procedure, such as total knee arthroplasty or anterior cruciate ligament reconstruction.

Interestingly, preoperative expectation scores were not correlated with final two-year PROMIS PI scores and only weakly correlated to change in PROMIS PI in our study. Prior literature shows inconsistent results regarding the relationship between expectations and postoperative PROs.⁵² This may be due to differences in methods of assessing expectations. Additionally, preoperative expectations may not correlate to postoperative pain in the same manner depending on the age group or procedure. One study speculated that an inverse relationship between expectations and PROs may also occur in the setting of unrealistically high preoperative expectations for patients undergoing anterior cruciate ligament reconstruction.⁵³ Fulfillment of expectations may be more predictive of postoperative PROMIS PI and should be investigated in future studies.

There are specific limitations to this study that readers must consider. A major limitation is the retrospective design of the study. It is impossible to determine causality with the level of certainty as would be achievable in an experimental study, or if the universe of possible confounders was known, collected, and controlled for. The utilization of surveys in this study was subject to loss to follow-up and non-response bias. However, this study had 73% two-year follow-up. Our study group may be subject to selection bias by virtue of our inclusion criteria and setting. Given that our data set was limited to surgical patients, our study conclusions do not apply to patients undergoing nonoperative treatment. To our knowledge, this is the largest cohort of patients undergoing knee surgery in which PROMIS PI was analyzed at two-years postoperatively. Characteristics of our study population were also a strength. Our cohort included a racially diverse group of patients from an urban academic medical center. And contrary to most studies in the orthopaedic literature, we reported on a heterogeneous group of procedures, making our findings widely applicable to the general orthopaedic community.

5. Conclusion

PROMIS PI two-years after knee surgery is associated with several preoperative psychosocial factors. Lower income, increased anxiety symptoms, smoking, greater knee pain, and lower activity were all associated with less robust PROMIS PI outcomes. Future studies can be aimed at investigating the potentially modifiable risk factors of worse postoperative pain interference.

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CRediT authorship contribution statement

Moli Karsalia: Investigation, Writing – original draft, Writing – review & editing. **Tina Zhang:** Project administration, Methodology,

Formal analysis, Writing – original draft, Writing – review & editing. **Ali Aneizi:** Project administration, Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Michael J Foster:** Writing – original draft, Writing – review & editing. **Matheus B Schneider:** Formal analysis, Writing – review & editing. **Patrick MJ Sajak:** Investigation, Writing – original draft, Writing – review & editing. **Vidushan Nadarajah:** Writing – original draft, Writing – review & editing. **Sean J Meredith:** Writing – original draft, Writing – review & editing. **R Frank Henn:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Visualization, Project administration, Funding acquisition.

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