

What Is the Relationship Between Depressive Symptoms and Pain During Functional Tasks in Persons Undergoing TKA? A 6-year Perioperative Cohort Study

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Abstract

Background Preoperative depressive symptoms have been shown in some but not all studies to be associated with poor self-reported pain and function outcomes. In addition, depressive symptoms after surgery have been shown to improve relative to preoperative levels.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Questions/purposes We hypothesized that (1) preoperative depressive symptoms would predict postoperative pain; (2) depressive symptoms would decrease after surgery; and (3) preoperative depressive symptoms would increase as the scheduled surgery date approached.

Methods Data from the Osteoarthritis Initiative, a National Institutes of Health-funded prospective multiyear cohort study, were used in this retrospective analysis. Persons from four communities were eligible if they had radiographic knee osteoarthritis or were at risk for developing knee osteoarthritis based on occupational, medical history, or body weight risk factors. A total of 4796 persons participated and rates of followup were 80% or greater over the course of the study. Participants completed a validated depressive symptom scale and the Knee Injury and Osteoarthritis Outcome Scale pain scale each year for 3 years before and 3 years after TKA. Latent growth curve modeling was used to model intercepts and slopes of pre- and postoperative depression and pain. Preoperative trajectories and intercepts were then used to predict postoperative pain and depressive symptoms adjusting for confounding variables.

Results After adjustment for potential confounding, we found no evidence that preoperative depressive symptoms predicted postoperative pain with function (estimate, 0.1; 95% confidence interval, -0.31 to 0.50; $p = 0.64$) or that depressive symptoms were reduced after surgery

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($z = 0.06$, $p = 0.80$). We also found no evidence to indicate that preoperative depressive symptoms increased as the date of surgery approached (linear slope = 0.28, SE = 0.19, $p = 0.15$).

Conclusions Preoperative and postoperative depressive symptoms in patients before and after TKA did not appreciably change over a 6-year perioperative period. Patient depressive symptoms were not reduced after surgery and did not appear to be related to less pain postoperatively. Our findings of no association between preoperative depressive symptom severity and postoperative pain and no reduction in postoperative depressive symptoms run counter to other available evidence, potentially attributable, in part, to a data collection process that occurred outside of orthopaedic surgeons' offices. Future research is needed to more fully explore the potential role of social desirability, the concept that patients respond in a way that they think the researcher or clinician wants them to respond in lieu of responding in a way that truly reflects the patient's status. Social desirability may influence a TKA patient's pain and function outcome assessment.

Level of Evidence Level I, prognostic study.

Introduction

TKA is a cost-effective procedure for patients with severe symptomatic knee osteoarthritis (OA) [13]. Despite high surgical success rates, as many as 25% of patients report compromised postoperative functioning and persistent pain although having a stable implant [2]. Recent research has indicated that psychologically based impairments and disorders such as pain catastrophizing, anxiety, and depression increase the risk of poor patient outcomes after TKA [3]. Measures of depressive symptoms tap the underlying construct of depression, but they also capture related symptoms such as anxiety and general emotional distress, which may manifest as difficulty sleeping, poor concentration, and negative feelings in patients. Given the conceptual overlap of depression, anxiety, and general psychological distress, negative thoughts and feelings associated with an impending major surgery can potentially inflate scores on questionnaire-based measures of depressive symptoms.

Our study focused on depressive symptoms and pain trajectories from three perspectives. First, elevated preoperative depressive symptoms have been shown to be prognostic of worse patient postoperative pain and poorer function [5, 6, 12, 17]. High levels of depressive symptoms likely make a challenging postoperative recovery even more difficult for patients and there is a moderate association between depression and pain [1, 7]. High preoperative depressive symptom scores also may indicate a

high patient risk of worse pain and function after surgery because of poor coping skills and a reduced ability to deal with the challenges of recovery. Despite the strong theoretic bases for elevated depressive symptoms leading to adverse health outcomes, it is not always the case [27]. Second, studies have reported reductions in depressive symptoms after surgery [5, 6, 12, 16] (Table 1), presumably indicating that surgical effects contributed to a reduction in depressive symptoms. Third, some patients may have mildly or moderately elevated preoperative depressive symptom scores because of the upcoming major surgery and all related health, lifestyle, and economic risks [15, 18]. We, therefore, determined whether preoperative depressive symptoms worsened as patient surgery date neared.

We tested three hypotheses related to perioperative depressive symptom and pain trajectories. First, we hypothesized that immediate presurgical depressive symptom scores would be associated with greater postoperative pain during functional tasks; that is, patients with higher (worse) preoperative depressive symptoms would have worse postoperative pain relative to patients with lower (milder) depressive symptoms. Second, to assess if surgery has a positive effect on depressive symptoms, we hypothesized that postoperative depressive symptom scores would be lower (indicating less depressive symptoms) than preoperative scores. Third, to assess the stressors of upcoming major surgery, we hypothesized that 3-year presurgical depressive symptom trajectories would indicate worsening depressive symptoms as the day of surgery approached.

Patients and Methods

Patients in our study were a subset of the 4796 patients enrolled in the Osteoarthritis Initiative (OAI), a National Institutes of Health, and privately funded, natural history, multicenter, prospective, 8-year longitudinal study of persons with or at high risk for knee OA [26]. The study was approved by the institutional review boards of each of the following participating OAI sites: the University of Maryland, Baltimore, MA, USA; the Ohio State University, Columbus, OH, USA; the University of Pittsburgh, Pittsburgh, PA, USA; and Memorial Hospital of Rhode Island, Pawtucket, RI, USA. No treatment was provided as part of the OAI, but patients were asked to self-report any treatments received in their communities.

Key study inclusion criteria were that patients be aged 45 to 79 years and have radiographic knee OA or one or more of several risk factors for knee OA. Patients were excluded if they had rheumatoid arthritis, had undergone bilateral knee arthroplasty (or preexisting plans to undergo bilateral knee arthroplasty in the next 3 years), bilateral

Table 1. Self-report depressive symptom scores in recent longitudinal studies of persons undergoing TKA

Study	Sample size	Depression scale	Mode of survey completion	Presurgery score (\pm SD)	Time*	Postsurgery score (\pm SD)	Postsurgery timeframe (months)
Duivenvoorden et al. [5]	133	HAD-S	Mailed	4.3 (3.8)	Unreported	3.4 (3.4) 3.1 (3.4)	3 12
Perruccio et al. [16]	494	HAD-S	Mailed	5.3 (3.5)	Average of 12 days	3.4 (3.3)	12.5
Edwards et al. [6]	43	CES-D	MD office	12.1 (6.8)	Unreported	13.9 (7.5) 11.8 (7.4) 9.8 (6.6) 7.8 (5.3)	1 3 6 12
Lopez-Olivo et al. [12]	241	DASS21	MD office	3.9 (5.8)	Within 1 month	2.2 (4.3)	6

* Time represents the number of days between the preoperative data collection session and the surgery day; HADS-D = Hospital Anxiety and Depression Scale–Depression Subscale; CES-D = Center for Epidemiologic Studies Depression Scale; MD = medical doctor; DASS21 = Depression, Anxiety, and Stress Scale–21 item version.

end-stage radiographic knee OA, or used ambulatory aids other than a single straight cane more than 50% of the time. In addition, men weighing more than 286 lbs and women weighing more than 250 lbs were excluded for technical reasons because they were unlikely to successfully undergo yearly MRI examinations required in the OAI protocol.

Patients provided yearly self-reported data and had annual radiographic, MRI, and performance-based evaluations, which were part of the OAI data collection. In our study, we used yearly data collected over a 7-year period, from baseline to the 7-year followup.

During the 7-year study period, a total of 386 patients underwent TKA. We excluded patients who underwent TKA and hip arthroplasty ($n = 15$), revision knee TKA ($n = 26$), or unicompartmental knee surgery ($n = 28$). We also excluded patients who underwent bilateral TKA, either in the same year or in different years ($n = 63$). These patients were excluded to reduce potential confounding and to study a patient group with isolated unilateral TKA and no other joint arthroplasty. Our final total number of study patients was 254, each of whom had undergone isolated unilateral TKA during the 7-year study period. Of all our study patients, 60% (154 of 254) were women; study patients had a mean age of 68 years; and 14.2% (36 of 254) were black (Table 2).

To assess outcome, we used yearly patient scores from the highly reliable and valid Knee Injury and Osteoarthritis Outcome Score (KOOS) pain scale [22, 23] for the surgical knees. The KOOS pain scale comprises nine items with a response range from 0 (severe function limiting pain) to 100 (no pain with function).

Depressive symptoms were quantified yearly during the study period by use of the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a 20-item validated scale with a score range from 0 to 60 with a score of 16 or higher generally accepted as the cut

Table 2. Characteristics of study patient population ($N = 254$)

Patient characteristics	Unilateral knee pain (mean \pm SD, range; or number [%])
Sex: women	154 (60.6)
Age (years; at surgery)	67.9 (8.6, 46–85)
Race	
White	210 (82.7)
Black	36 (14.2)
Other	8 (3.1)
Body mass index (kg/m^2)	30.0 (4.6, 21.1–43.5)
Comorbidity	0.43 (0.8, 0–4)
Preoperative	
Depressive symptoms	7.3 (6.9, 0–37)
KOOS pain score	55.5 (18.2, 8.3–100)
WOMAC function score	25.0 (12.3, 0–68)

KOOS = Knee Injury and Osteoarthritis Outcome.

score indicating probable clinical depression [3, 9, 11, 19]. The CES-D is often used to study community-based, elderly persons and has recently been endorsed by Smarr and Keefer [24] for use in patients with arthritis.

We used age, gender, body mass index (BMI), and comorbidity as covariates because of their potential role in influencing the outcome/depressive symptom relationship. BMI was calculated using the standard method of weight in kilograms divided by height in meters². Comorbidity was quantified with a validated modified Charlson comorbidity index [10].

Data Analysis

Latent growth curve modeling was used to determine pre- and postsurgical trajectories for pain and depression

separately. The models were required to test the three hypotheses. Latent growth curve modeling has the advantage of accounting for individually varying times of observation, efficient handling of missing-at-random data through maximum likelihood estimation, and allowing for estimation of random slopes and intercepts. As a result of only three time points for each model, quadratic term variance was fixed at zero.

Once the individual models were determined, intercept and linear slope for depression and pain, with significant variance presurgery, were used to predict each intercept and linear slope postsurgery for both depression and pain outcome variables controlling for the previously described covariates. Each of the terms was included in the model simultaneously, thus controlling for the effect of the other variables in the model. Coefficients with nonsignificant variances were excluded in the model fitting, which allowed for the examination of how the elevation (intercept) and change (slope) in presurgery depressive symptoms predict the elevation and change in postsurgery depressive symptoms and pain.

The statistical model designed to predict postoperative pain from preoperative depressive symptoms was used to test hypothesis 1 (patients with higher [worse] preoperative depressive symptoms would have worse postoperative pain relative to patients with lower [milder] depressive symptoms), whereas the pre- and postoperative depressive symptom model was used to test hypothesis 2 (postoperative depressive symptom scores would be lower [indicating less depressive symptoms] than preoperative scores). The latent growth curve model for preoperative depression was used to test hypothesis 3 (presurgical depressive symptom trajectories would indicate worsening depressive symptoms as the day of surgery approached).

We had minimal loss to followup. The number of persons with missing depressive symptom scores during each data collection session was as follows: 5% (10 of 205) had missing data at the 3-year pre-operative period, 4% (10 of 235) had missing data 2 years preoperatively, 6% (14 of 254) had missing data at the 1-year preoperative session, and 5% (12 of 254), 9% (19 of 206), and 16% (26 of 167) has missing data at the 1-year, 2-year, and 3-year postoperative sessions, respectively.

Results

We found that patients with worse preoperative depressive symptoms did not have worse postoperative pain compared with patients with milder depressive symptoms after adjusting for potential confounders ($\beta = 0.10$; $p = 0.64$; 95% confidence interval [CI], -0.31 to 0.50 ; Table 3). The 95% CI suggests that fairly large changes

in depressive symptoms (eg, several points) would likely not result in clinically important KOOS pain changes and combined with the p value of 0.64, our data indicate that the association between preoperative depressive symptoms and postoperative KOOS pain is very weak at best (Figs. 1, 2). Figure 1 illustrates the mean depressive symptoms scores, with 95% CIs, over the study period, whereas Fig. 2 illustrates the mean KOOS pain scores over the same period.

We found that preoperative depressive symptom intercept and postoperative depressive symptom intercept were strongly associated, after adjusting for potential confounders, with the β intercept = 0.83 and a $p < 0.001$ (Table 3). There was no significant difference in mean levels of depression ($z = 0.06$, $p = 0.80$) before and after surgery. These data indicate that preoperative and postoperative depressive symptoms were strongly associated with one another and essentially unchanged after surgery (Fig. 1). This lack of change association is illustrated in Fig. 1.

A nonsignificant slope for preoperative depressive symptoms was seen (estimate, 0.02, $p = 0.99$) (Table 4). The data indicated that preoperative depressive symptoms were unchanged during the preoperative 3-year period and, contrary to our hypothesis, depressive symptoms did not worsen as the time of surgery approached (Fig. 1).

Discussion

The study of psychological distress in patients undergoing TKA has received increased attention and some studies have suggested that elevated preoperative depressive symptoms are prognostic indicators of worse pain and function outcome after surgery. In addition, depressive symptoms have been shown to decrease after surgery [5, 6, 12]. However, other studies have suggested depressive symptoms have little influence on pain or function postoperatively [21, 25]. Our study was hypothesis-driven because several studies have reported inconsistent findings related to the prognostic value of preoperative depressive symptoms and the extent to which depressive symptoms change from the pre- to the postoperative period [5, 6, 12, 16, 17]. We found that preoperative depressive symptoms were not prognostic of the extent of postoperative pain and that the extent of depressive symptoms was essentially unchanged after surgery. We also found that preoperative depressive symptoms did not worsen as the surgery date neared.

Our study had limitations, and our findings cannot be directly compared with other studies [5, 6, 17, 27] for a variety of reasons. Our data were collected from OAI, a natural history knee OA study unlike other studies examining the prognostic importance of postoperative

Table 3. Predicting postsurgical trajectories from pre-surgical trajectories controlling for age, body mass index, comorbidity, and sex

Postoperative	Preoperative	Estimate (95% confidence interval)	SE	Z	p value
Depression Intercept	Depression intercept	0.83 (0.69–0.96)	0.07	11.79	< 0.001
	Pain intercept	−0.002 (−0.04 to 0.04)	0.02	−0.10	0.92
	Pain linear	0.02 (−0.09 to 0.12)	0.05	0.332	0.74
Pain Intercept	Depression intercept	0.10 (−0.31 to 0.50)	0.21	0.46	0.64
	Pain intercept	0.45 (0.27–0.63)	0.09	4.85	< 0.001
	Pain linear	0.27 (−0.10 to 0.63)	0.19	1.42	0.15

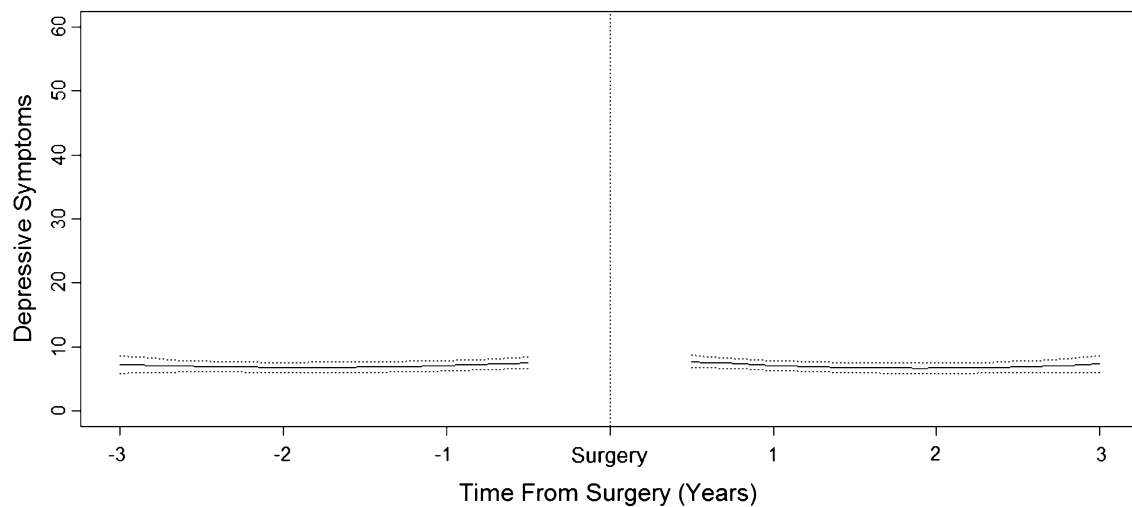
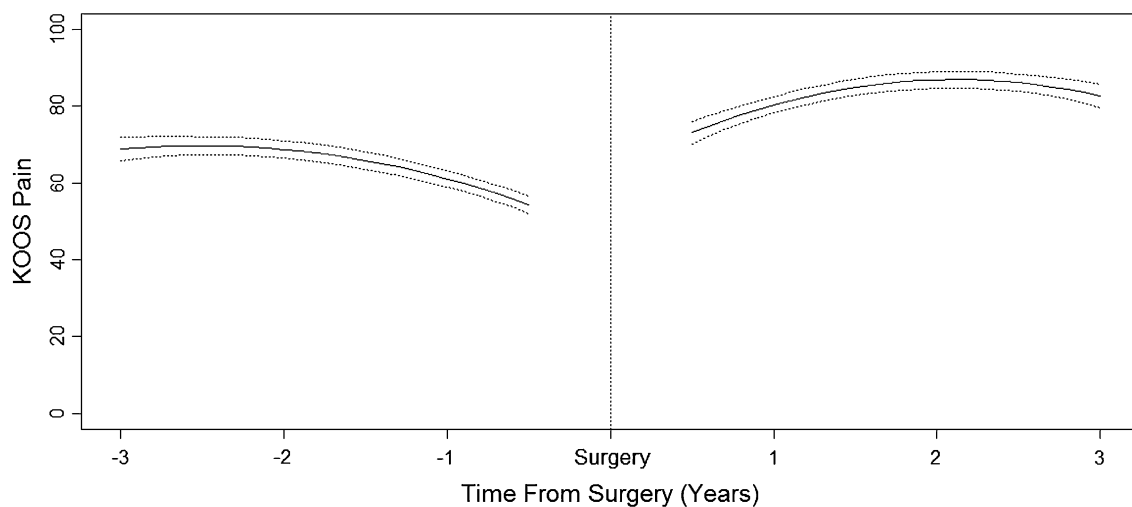
**Fig. 1** The CES-D depressive symptom growth curves for the 3-year period both before and after TKA are illustrated in Fig. 1. Curves are adjusted for age, gender, BMI, and comorbidity.**Fig. 2** The KOOS pain score growth curves for both the 3-year period before and after TKA are illustrated in Fig. 2. Curves are adjusted for age, gender, BMI, and comorbidity.

Table 4. Latent growth curve model results for pain and depression pre- and postsurgery

	Presurgery			
	Estimate	SE	Z	p value
Pain means				
Intercept	65.85	1.15	57.04	< 0.001
Linear	−7.68	0.66	−11.64	< 0.001
Quadratic	−3.81	0.73	−5.21	< 0.001
Pain variances				
Intercept	187.59	22.60	8.30	< 0.001
Linear	46.16	17.49	2.64	0.01
Depression means				
Intercept	6.81	0.42	16.27	< 0.001
Linear	0.28	0.19	1.43	0.15
Quadratic	0.37	0.34	1.11	0.27
Depression variances				
Intercept	30.13	4.14	7.27	< 0.001
Linear	0.02	2.62	0.01	0.99
	Postsurgery			
	Estimate	SE	Z	p value
Pain means				
Intercept	84.84	1.10	76.97	< 0.001
Linear	6.36	0.84	7.54	< 0.001
Quadratic	−5.26	0.85	−6.20	< 0.001
Pain variances				
Intercept	159.08	24.87	6.40	< 0.001
Linear	33.60	21.65	1.55	< 0.121
Depression means				
Intercept	6.74	0.41	16.61	< 0.001
Linear	−0.42	0.27	−1.54	0.12
Quadratic	0.50	0.32	1.55	0.12
Depression variances				
Intercept	23.96	3.52	6.80	< 0.001
Linear	0.67	4.08	0.17	0.87

SE = standard error for the parameter estimate.

changes in depressive symptoms of patients undergoing TKA. Most studies collected data after patients consented to undergo TKA and patients were recruited directly from orthopaedic surgeon offices within a few days or weeks of the surgery. That said, we believe our study to be a potentially less biased reflection of patients' depressive symptom status over an extended period, both before and after undergoing TKA. Because of the OAI design, potential biases associated with the recruitment of patients directly from orthopedic surgeons' offices and immediately before a presumably emotionally distressing event (TKA) were minimized. Our sample size was not large but our parameter estimates that we used to test our hypotheses had what we believed to be reasonably strong precision to

support our conclusions. Furthermore, our estimated effects were small and even if they were found to be statistically significant, it is unlikely they would be clinically relevant. Some prior studies have reported the timeframe for collecting patient preoperative depressive symptoms data, and, on average the studies collected data 12 days from surgery [17] and within a month of surgery [12]. Our study is limited in this regard because of the OAI time-varying design. For the 254 patients in our study, depressive symptom data were collected at a mean of 176 (\pm 99) days before surgery and a total of 21.5% of our study patients ($n = 54$) were assessed within 90 days of surgery. The Pearson product moment correlation coefficient between the number of preoperative days and the preoperative depressive symptom scores was 0.15 indicating that explained variance between the two measures was only 2.3%. These data suggest that the relationship between number of days before surgery and preoperative depressive symptom severity is extremely weak and in our view unlikely to influence the findings. With that said, our study likely had a limited ability to capture increased psychological distress attributable to the impending surgery. Pain in other joints may influence outcome after TKA [17] and we did not account for this source of variation in the analysis.

A total of 11.8% of our patients had preoperative CES-D scores of 16 or higher. A total of 20.3% of the patients in the TKA study by Duivenvoorden and colleagues [5] met the criteria for clinical depression. These data suggest our patients, on average, had preoperative depressive symptoms that were somewhat less intense than those reported in some studies that examined the prognostic importance of preoperative depressive symptoms.

Regarding the prognostic importance of preoperative depressive symptom scores, we found no association between patient preoperative depressive symptoms and postoperative pain. We found that preoperative depressive symptoms trajectories were not prognostic for the postoperative pain trajectories. Other reports found depressive symptoms to be prognostic for postoperative pain [5, 6, 12, 17], but others did not [4, 21, 25]. We also found that patient depressive symptom scores did not improve after surgery. Several studies have found that depressive symptom scores are lower (indicating less intense depressive symptoms) after surgery [5, 6, 12, 16].

Reasons for the differences between our study and prior reports could be the result of (1) the use of different instruments to measure depressive symptoms; (2) the spectrum of severity of preoperative depressive symptoms; or (3) the context in which the studies measured depressive symptoms. Studies that found prognostic use for preoperative depressive symptoms used a variety of depressive symptom measures, including the Hospital

Anxiety and Depression Scale [28], the Depression, Anxiety and Stress Scale [14], and the CES-D [19]. These instruments have all been extensively validated for quantifying depressive symptoms [24], making it unlikely that instrument choice had a substantial impact on our findings.

The mean preoperative CES-D depressive symptom severity in our study was 7.3 (\pm 6.9) on a 0 to 60 scale. Clinical depression is likely, with a sensitivity of 89% and specificity 86%, when the CES-D score is 16 or higher [8]. Our study patient mean score was slightly below half the score required for clinical depression and below the mean CES-D score (12.1 ± 6.8) of the patients studied by Edwards and colleagues [6]. It is unclear, however, whether less intense depressive symptoms in our sample explain why we found no prognostic significance for depressive symptoms.

The context in which measurements were obtained in our study was, in our view, the most likely explanation for the findings. Studies that have examined psychological distress and TKA typically have recruited patients directly from orthopaedic surgeons' offices, whereas OAI participants were recruited from the community without regard to medical or surgical care received and the great majority of patients were recruited a few to several years before undergoing TKA. It is possible that OAI patients did not associate OAI participation with their surgical care, whereas patients recruited directly from surgeons' offices may be more vulnerable to social desirability bias, which could influence self-rating of their symptoms. For example, patients participating in studies affiliated with orthopaedic surgeons' offices may associate their responses more closely to their experiences and satisfaction with the surgery or the surgeon and support staff and this suspected association may have biased responses [20]. Participants in OAI may have responded to questionnaires with less bias because the OAI is not affiliated with surgeons who conducted the surgeries. This is, however, speculative and more research is needed to adequately explore whether social desirability effects could have an impact on responses of patients undergoing TKA.

Our findings regarding the prognostic importance of depressive symptoms and postoperative changes ran counter to a fairly substantial literature in that we found depressive symptoms were not prognostic of postsurgical pain or depressive symptom improvement. During the years before and after TKA, depressive symptoms in our patients were essentially unchanged despite substantial reductions in pain experienced during functional tasks. Depressive symptoms were not prognostic for poor outcome and may not be an important, modifiable risk factor for future pain reduction in patients, particularly in patients with low or moderately elevated depressive symptom scores before undergoing TKA. Clinicians should focus on

identification of preoperative patients with clinical depression for potential treatment and not be as concerned about patients with low to moderate levels of depressive symptoms.

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