Multiple joint involvement in total knee replacement for osteoarthritis - effects on patient-reported outcomes

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Multiple joint involvement in total knee replacement for osteoarthritis - effects on patient-reported outcomes

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Objective: To determine whether symptomatic (painful/problematic) joints pre total knee replacement surgery (TKR), 1) influence pre and 12-month post-TKR patient-reported outcomes (pain, physical function, mood (fatigue, anxiety, and depression)); and 2) influence post-surgical pain and function mediated through mood.

Methods: 494 participants completed the identified patient-reported outcome measures pre- and 12-months post-TKR. Symptomatic (painful/problematic) joints were indicated on a homunculus pre-surgery. Covariate data included age, sex, educational attainment, BMI and comorbidity. Pre- and post-surgical outcome scores were regressed on symptomatic joint sites and covariates using linear regression analyses; post-surgical scores additionally were regressed on pre-surgery scores. Path analyses examined whether the effects of symptomatic joint sites on post-surgical pain and function were mediated through mood.

Results: Age range: 35-88 years (mean=65) with 65% female. Forty-six percent reported ≥ 4 symptomatic joints (other than surgical knee). Pre- and post-surgery, worse outcome scores were observed with increasing joint count. Adjusted for covariates, individuals reporting ankle/feet/toes, neck and spine/lower-back had worse pre-surgery fatigue and anxiety. Adjusted for covariates and pre-surgery status, worse fatigue for neck and spine/lower back, and worse depression, pain and function for ankle/feet/toes and neck were observed post-surgery. The influence of ankle/feet/toes on post-surgical pain and function was in part direct and partially mediated through depression. Full mediation was found for neck through fatigue, anxiety and depression and for spine/lower back through fatigue.

Conclusions: Findings suggest a comprehensive approach to OA management/care are warranted, and identify important associations between symptomatic joints and mood which negatively impact post-TKR pain and physical function.

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Significance and Innovations.

- Multiple symptomatic joints were highly prevalent in this OA total knee replacement population and were associated with worse patient-reported outcomes (pain, physical function, and mood (fatigue, anxiety and depression)) both pre- and post-TKR.
- Mood played an important mediating role between symptomatic joints and post-TKR pain and physical function.
- These findings may help explain some of the variability observed in post-TKR outcomes across patients and suggests a holistic approach to OA management is warranted.
- Knowledge that a patient has multiple symptomatic joint involvement prior to surgery may be used to educate the patient, allowing for more realistic expectations to be set and the need for adoption of self-management strategies, pre- and post-surgery, to be more apparent.

When conservative treatment fails for hip or knee osteoarthritis (OA), total joint replacement (TJR) is an elective surgical option that can provide significant pain relief and improved function with proven cost-effectiveness^{1;2}. Patient-reported outcomes are indispensable in evaluating TJR². By far, the focus of patient-reported outcomes studies in TJR have been on pain and function; not surprising as these are the key indicators for surgery^{1;3;4}.

Several literature reviews have reported on the determinants of patient-reported pain and physical function outcomes for primary TJR for OA. Evaluating demographic and socioeconomic characteristics, and pre-operative comorbidity and pain and function as determinants of post-operative pain and function has been the predominant focus^{1;3;4}. Patient expectations and pre-operative psychological status also have been assessed as predictors of post-operative pain and function and health-related quality of life generally⁵⁻⁹. While TJR has been shown to be highly effective for relieving the pain and ameliorating the limited function associated with hip and knee OA, significant variability in the degree of improvement in these outcomes following primary TJR have been noted^{3;4;10}. Generally, the extent to which these factors have explained post-TJR outcomes has been modest¹.

OA can simultaneously affect multiple joints in the body¹¹. Yet, the influence of multiple symptomatic joints is not routinely considered in OA studies which enroll patients or participants based on OA in a specific joint. This is particularly the case for studies assessing patient-reported outcomes in cohorts undergoing total joint replacement (TJR) for OA. Since multiple joints can be affected in OA, and given the complex involvement of many joints in lower extremity function, we posit that the presence of multiple symptomatic joints in TJR populations negatively influences lower extremity pain and function, and thus potentially may explain some of the

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variability in these post-surgical patient-reported outcomes. In other words, the surgical intervention on the hip or knee is but one component in the management of lower extremity symptoms and limited function associated with the disease.

Several studies also have identified an association between poorer pre-TJR mood (fatigue, anxiety, and/or depression) and poorer post-surgery outcomes⁵⁻⁹. Additionally, studies have generally identified an association (some suggest bidirectional), between mood and levels of pain and physical function, including in OA^{8;12-14}. Thus, we further posit that the presence of multiple symptomatic joints may influence pre-and post-surgical levels of pain and function in part through mood.

In this study, we consider the influence of specific symptomatic joints in a total knee replacement (TKR) cohort on 1) pre-surgery pain and function; 2) pre-surgery mood; 3) post-surgery levels of pain and function and mood; and 4) examine whether the influence of symptomatic joints on post-surgical pain and function are mediated through mood.

PATIENTS AND METHODS

Individuals undergoing primary unilateral TJR for knee OA were recruited from four Toronto, Canada academic hospitals. Eligibility criteria included 18 years of age or older and ability to read and comprehend English. Individuals having surgery for other than osteoarthritis or revision-arthroplasty were ineligible.

The study was approved by the University Health Network Research Ethics Board (REB) and the REB of each participating institution. Written informed consent was obtained from all study participants. Mailed health questionnaires were completed pre-surgery and at 12 months post-surgery.

Painful joints. Prior to surgery only, study participants were asked to indicate on a homunculus all joints that were painful or problematic and affected by arthritis.

Pain on activity and limitations in physical function were assessed with the Western Ontario McMaster University Osteoarthritis Outcome Index (Likert version 3.0) (WOMAC)¹⁵. The WOMAC is one of the most often used lower extremity patient-reported pain and function measures used in hip and knee TJR. The measure assesses the frequency and extent of pain during activities such as 'walking on a flat surface' and 'going up/down stairs' and assesses individuals' ability to move around and look after themselves, eliciting the degree of difficulty experienced due to their knee. The measures have documented reliability, validity and responsiveness in TKR^{15;16}. Pain scores can range from 0-20 and physical function from 0-68; higher scores indicate worse status.

Fatigue was assessed with the Profile of Mood States fatigue subscale¹⁷. The POMS is a frequently used measure of fatigue in the literature and has been used to study fatigue in a range

of chronic conditions. The POMS has documented validity¹⁸ with scores ranging from 0-20; higher scores indicate worse status.

Anxiety and *Depression* were captured with the Hospital Anxiety and Depression Scale¹⁹. The HADS has been widely used in outpatient populations, and the reliability of each subscale is sufficient for group comparisons in multiple populations²⁰.

Pain, limitations in physical function, fatigue, anxiety and depression measures were administered at both time points. Collected pre-surgery were: *Comorbidity* (individuals responded yes/no to a list of 14 medical problems identified in the Self-Administered Comorbidity Questionnaire²¹), *age* at surgery, *sex*, level of *education* ($\leq$ high-school, $\geq$ post-secondary), and height and weight, used to calculate body mass index (overweight ($25 \leq \text{BMI} < 30$); obese ($\text{BMI} \geq 30$)).

Analyses

The demographic, obesity, comorbidity and painful joint location profile of the sample was described and tetrachoric correlations between joint sites were calculated. As well, pre-surgery and 12-month post-surgery scores for all study measures were documented for the overall sample and by symptomatic joint count (other than the surgical knee): 0 (i.e. surgical knee only); 1 to 3; and 4 or more. A test for trend for each study measure was conducted both pre- and post-surgery by symptomatic joint count. Linear regression analyses were used to examine the influence of painful joint involvement (by location) on pre-surgery and 12-month post-surgery scores for each study measure. Regression models were adjusted by age at surgery, sex, level of education, overweight and obesity, and comorbidity count. For the models where the post-surgical score was the dependent variable, pre-surgery scores for the respective measures were also included as

predictors. As multiple comparisons were undertaken, Bonferroni adjustment, including a correction for correlated outcomes, of critical p-values was utilized for the linear regressions. With this adjustment, p-values ≤ 0.027 were considered statistically significant, and the z-value for 2-sided testing equaled 2.21.

To test our hypotheses, and dependent on whether the linear regressions results suggested that painful/problematic joints influenced pre- and post-surgical pain, physical function and mood scores, path analyses were undertaken to assess the possibility that the effects of pre-surgery painful/problematic joints on post-surgical pain and physical function were mediated through mood. Figure 1 diagrammatically presents the hypothesized mediated model. While all models included age, sex, level of education, overweight/obese, and comorbidity count, these are not shown in the diagram. Two models were assessed such that the influences of painful/problematic joint sites on post-surgery pain (Model 1) and physical function (Model 2) scores were specified both as direct and indirect (through post-surgery fatigue, anxiety and depression) effects. Direct effects from pre-surgery scores to respective post-surgery scores were specified for all measures. Additionally, the influence of pre-surgery mood on post-surgery pain and physical function was specified as both direct and indirect (through post-surgery mood). Different indices provide different information about model fit. Five indices were considered: model χ^2 , root mean square error of approximation (RMSEA), comparative fit index (CFI), Tucker-Lewis index (TLI) and the standardized root mean square residual (SRMR). Good fit was supported by a non-significant χ^2 (i.e. $p > 0.05$), and values ≤ 0.05 , ≥ 0.95 , ≥ 0.95 , and ≤ 0.08 , respectively. To identify potential focal areas of misfit in the model, standardized covariance residuals also were examined, with values > 2.58 interpreted as misfit (i.e. significant residual). Analyses were carried out using SAS 9.2 for the linear regressions and Mplus 6.1 for the path

analyses.

Sample size adequacy was assessed using two approaches suggested in the literature for structural equations modeling. The first was based on the requirement of at least five subjects per parameter to be estimated^{22;23}. Based on our hypothesized path model, comprised of 67 parameters to be estimated, this would require an $n \geq 335$. The other approach was based on using the RMSEA as effect size. Specifically, it was based on a test of the null hypothesis of close fit (RMSEA = 0.0 for exact fit) versus the alternative hypothesis of not close fit (RMSEA of 0.05)^{24;25}. In our case, our n provided power=81.2%

RESULTS

494 patients participated in the study and provided baseline data. Across study measures, a minimum of 435 provided 12-month data. Table 1 presents a description of the study sample. The majority of participants were female (65%) and the mean age of the sample was 65 years, with ages ranging from 35 to 88 years. The majority of the sample reported greater than high school education and just less than half of the sample had a BMI value indicative of obesity. The vast majority (85%) reported a painful joint other than their surgical knee on the homunculus, with nearly half the sample reporting four or more painful/problematic joints. The most frequently reported joint was the contralateral knee, followed by elbow/wrists/hands. One-third of the sample reported symptomatic ankles/feet/toes, and spine/lower back. One-fifth of the sample reported their neck as painful/problematic. Tetrachoric correlations between joint sites (data not shown) ranged from 0.06 to 0.6, with the smallest between contralateral knee and hips and largest between neck and spine/lower back.

Pre-surgery and 12-month scores for the patient-reported outcomes are presented in Table 2 for the overall sample and by symptomatic (other than surgical knee) joint count; higher scores represent worse status. Statistically significant trends were observed, with lower scores (i.e. less pain and functional difficulties) among individuals who reported no joints other than their surgical knee and higher scores among those reporting 4 or more symptomatic joints. These trends were consistent for both the mood and knee-specific measures at all times.

Results from the linear regression analyses examining pre-surgery scores are presented in Table 3. Adjusted for age, sex, education, overweight/obese, comorbidity count, and all joint sites, individuals reporting foot/ankle/toes, neck, and spine/lower back had worse pre-surgery

fatigue and/or anxiety scores compared to those not reporting these joint sites. Individuals reporting painful/problematic shoulders had worse pre-surgery scores for WOMAC pain.

From our second set of linear regressions, pre-surgery scores were found to be significantly associated with 12-month scores across all measures (Table 4). Consistently, higher pre-surgery scores predicted higher post-surgery scores; the magnitudes of the betas, however, are consistent with overall improvements over the 12-month recovery period for all measures. Adjusted for pre-surgery scores, individuals who reported ankle/feet/toes had worse post-surgery scores for depression and WOMAC pain and physical function. Individuals reporting painful/problematic neck had worse post-surgery scores for fatigue, depression and WOMAC pain and physical function. Finally, individuals reporting painful/problematic spine/lower back had worse scores for fatigue. The percent of variance explained for each of these post-surgical outcomes ranged from 27% to 45% for mood, and was 20% and 29% for WOMAC pain and physical function.

Although the magnitudes of the correlation coefficients were not suggestive of any high collinearity, variance inflation factors (VIF) for joint sites were nevertheless examined in the above linear regressions to ensure that multicollinearity was not a problem. The largest VIF encountered across all models (data not shown) was 1.39, far below accepted cutoff values of 10 and even more stringent cutoffs of 2.5^{26;27}, suggesting multicollinearity was not a concern.

Both path analytic models displayed very good overall model fit without localized areas of strain. For Model 1 (examining post-surgery WOMAC pain): model $\chi^2=18.189$ (Prob($\chi^2_{15}>18.189$)= 0.2529), RMSEA=0.023 (Prob(RMSEA $\leq$ 0.05)=0.904), CFI=0.997, TLI=0.986, SRMR=0.011 and standardized covariance residuals $<|\pm 1.8|$. For Model 2 (examining post-surgery WOMAC physical function): model $\chi^2=18.59$ (Prob($\chi^2_{15}>18.59$)= 0.2329), RMSEA=0.025 (Prob(RMSEA $\leq$ 0.05)= 0.895), CFI=0.997, TLI=0.985, SRMR=0.010,

and standardized covariance residuals $<|\pm 1.8|$.

Results from the path analyses (Table 5) indicated that the influence of ankle/feet/toes on post-surgical pain and physical function scores were partially direct and partially mediated through post-surgery depression. No other direct effects of joint sites on post-surgical pain and function were found to be significant. However, painful/problematic neck was found to be significantly associated with post-surgery levels of anxiety, depression and fatigue, and painful/problematic spine/lower back with post-surgical levels of fatigue (in all cases, reporting of the joint site was associated with worse scores). Post-surgical levels of depression and fatigue were in turn associated with post-surgical levels of pain and physical function (higher levels of depression and fatigue associated with worse pain and physical function), and improvement in depression scores was associated with better post-surgical pain levels. Thus, the results suggest the effects of ankle/feet/toes (partially) and neck and spine/lower back (fully) were mediated through mood. The percent of variance explained for post-surgical pain was 43.5% and 54% for physical function.

DISCUSSION

Joint pain has been identified as an important determinant of overall health status and level of disability in population studies²⁸⁻³¹. OA affects many joints, often in combination, yet the influence of multiple symptomatic joints has received limited attention in joint-specific OA cohorts, particularly TKR cohorts. The goal of this investigation was to determine whether the presence of painful/problematic joints pre-surgery influenced patient-reported outcomes prior to and following TKR for OA and to understand how multiple joint involvements might influence pain and physical functional status.

It was the norm, not the exception, in this knee OA cohort for multiple painful joints to be reported. Nearly half the sample reporting in excess of three joints other than the surgical knee, and at least one-third reported each of at least one upper and one lower extremity joint. When considering the influence of painful joints on post-surgical outcomes, the focus has been predominantly on the contralateral joint and on low back pain, and these influences have predominantly been examined in total hip replacement³²⁻³⁶. Consistently, painful symptoms in the contralateral joint and in the lower back have been associated with worse post-surgical pain and physical function status in these cohorts.

Our work points to a significant influence of specific symptomatic joints on post-TKR pain and function, including the ankle/feet/toes, spine/lower back and neck. Given that the WOMAC pain and physical function questions elicit responses for daily activities in which the feet and ankles play a critical role (e.g. walking on a flat surface), it is not surprising that poorer scores were observed for individuals reporting ankle/feet/toes as being painful or problematic. In a study examining activity levels following TKR, Dahm et al. reported that study participants cited other problematic joints as limiting their activity³⁷. Of these, the hip, opposite knee and

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3 foot/ankle were most frequently cited. Our findings from the path analyses show the only joints
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5 which had direct effects on post-surgery pain and function scores were the ankle/feet/toes.
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7 Additionally, the influence of pain in these joints was found to be mediated through mood,
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9 particularly depression.
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13 The association of upper extremity problematic joints, and particularly the neck, with lower
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15 extremity post-surgery pain and function in this cohort was not initially obvious. However,
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17 results from the path analyses revealed an important relationship between the reporting of neck
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19 and spine/lower back as painful/problematic and poorer mood status, and then through to lower
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21 extremity pain and function post-surgical scores. These effects were fully mediated through the
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23 mood indicators, either through anxiety (neck), depression (neck) or fatigue (neck and
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25 spine/back). Although previous studies have not considered such mediated path models in this
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27 population, these findings are consistent with studies identifying poorer psychological status as a
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29 risk factor for musculoskeletal pain and disability^{28;38-41}. Poorer pre-surgery psychological
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31 status or mood has been associated with worse pain and physical function status post-surgery
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33 1;4;8;42. As well, a number of studies have reported an association between higher levels of
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35 anxiety, depression, and/or fatigue and poorer pain and physical function status, and suggested
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37 that these relationships may be bidirectional¹³. In a community sample of individuals with
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39 lower extremity OA, Hawker et al. similarly reported on the impact of pain on later depression
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41 and fatigue and subsequently on worsening pain¹². Power et al. reported that individuals with
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43 lower extremity OA identified fatigue as both being influenced by and influencing later
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45 experiences of pain and disability¹⁴.
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53 These associations may be a critical link, therefore, in understanding the variability observed
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55 among individuals with specific painful joint sites. The high prevalence of multiple symptomatic
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joints in this TKR population suggests that systemic effects may be operational in OA, with negative consequences on lower extremity pain and function and overall indicators of mood. These findings support a more holistic approach to OA management⁴³, with a view that joint replacement is but one part of the potential package of care and management. Conceivably, these findings highlight a need for OA-specialist care. Additionally, for the surgeon, knowledge that the patient has multiple painful joint involvement prior to surgery may be used to educate the patient, allowing for more realistic expectations to be set and the need for adoption of self-management strategies, pre- and post-surgery, to be more apparent.

A limitation of this study is that it was limited to a knee OA cohort. Whether similar associations, frequency of multiple symptomatic joint involvement, and similar joint-specific prevalence estimates would be identified in other joint-specific OA cohorts is unclear. However, similarities in conclusions between studies of community samples with OA and our knee OA cohort suggest that similar patterns of effects may be operational. Also, our sample was limited to patients recruited from academic hospitals. We note, however, that a recent study⁴⁴ compared patient-reported functional outcomes following primary TKR between surgeries performed in 5 academic and 5 community hospitals. Differences in pain and function and patient quality of life were not detected between the groups at any of the study time points. This suggests that post-surgical trajectories of functional status and quality of life in the present sample are likely to be typical of primary TKR outcomes more generally.

Multiple symptomatic joint involvement in OA is well established. Our findings suggest a comprehensive approach to OA and musculoskeletal comorbidity management and care are warranted, and identify important associations between painful joints and mood which ultimately negatively impact post-surgical TKR outcomes, and overall health-related quality of life.

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Table 1. Sample descriptives*.

	Mean (range) or Proportion
Age	64.9 (35, 88)
Sex: Female	65.4%
Education: ≤high school	40.7%
Body mass index:	
overweight (25≤BMI<30)	37.9%
obese (BMI≥30)	45.3%
Comorbidity count	1.5 (0, 6)
Painful/problematic joints	
Surgical joint only	15.2%
Not including surgical joint	
Count	5.1 (1, 19)
1	16.6%
2	12.8%
3	9.9%
4+	45.5%
Contralateral knee	57.1%
Elbow/Wrists/Hands	49.0%
Ankle/Feet/Toes	36.0%
Spine/lower back	30.6%
Shoulders	29.4%
Hips	24.7%
Neck	21.7%

*N ranges from 471 to 494 for individual characteristic responses.

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Table 2. Health measure scores*†, pre-surgery and 12-months post-surgery; overall and by symptomatic joint count.

			Symptomatic Joint Count (other than surgical knee)				
			Overall sample Mean (sd) (n=494)	0 Mean (sd) (n=75)	1-3 Mean (sd) (n=194)	4 or more Mean (sd) (n=225)	p-value for test of trend
Pre-surgery	Fatigue	7.9 (5.6)	5.9 (4.4)	7.0 (5.5)	9.5 (5.5)	<0.0001	
	Anxiety	6.5 (4.0)	6.2 (4.1)	5.6 (3.6)	7.3 (4.1)	<0.0001	
	Depression	5.3 (3.5)	4.8 (3.7)	4.9 (3.4)	5.7 (3.5)	0.0299	
	Pain	10.5 (3.6)	9.7 (3.6)	10.1 (3.6)	11.0 (3.4)	0.0094	
	Physical Function	33.9 (12.6)	31.1 (12.7)	32.0 (12.9)	36.3 (11.9)	0.0003	
Post-surgery	Fatigue	5.4 (4.8)	4.4 (4.0)	4.3 (4.5)	6.7 (5.0)	<0.0001	
	Anxiety	4.4 (4.0)	3.8 (3.4)	3.7 (3.9)	5.3 (4.2)	0.0003	
	Depression	3.4 (3.3)	2.6 (2.7)	3.0 (3.1)	4.1 (3.6)	0.0007	
	Pain	3.4 (3.3)	2.6 (2.7)	3.1 (3.4)	4.0 (3.4)	0.0046	
	Physical Function	13.9 (11.3)	10.9 (9.0)	12.5 (11.5)	16.2 (11.4)	0.0004	

*Higher scores indicate worse status.

†Possible score range: Fatigue (0-20); Anxiety (0-21); Depression (0-21); WOMAC pain (0-20) and physical function (0-68).

Table 3. Linear regression results; outcome: pre-surgery patient-reported outcome score (statistically significant effects are bolded)*

Predictors	Model Outcome				
	Fatigue	Anxiety	Depression	Pain	Physical Function
Beta (Confidence Interval)					
Age	-0.11	-0.09	-0.09	-0.10	-0.18
	(-0.16, -0.05)	(-0.13, -0.05)	(-0.13, -0.06)	(-0.14, -0.07)	(-0.31, -0.06)
Gender (ref: female)	-1.37	-0.85	-0.61	-1.08	-3.47
	(-2.55, -0.19)	(-1.68, -0.01)	(-1.36, 0.13)	(-1.82, -0.35)	(-6.08, -0.86)
Education	1.17	1.47	0.69	1.18	4.83
(ref:>high school)	(-0.02, 2.36)	(0.64, 2.31)	(-0.06, 1.44)	(0.44, 1.92)	(2.22, 7.44)
BMI (ref: normal)					
Overweight	-0.42	-0.38	-0.01	-0.13	1.69
	(-1.99, 1.16)	(-1.50, 0.74)	(-1.01, 0.99)	(-1.13, 0.86)	(-1.83, 5.20)
Obese	1.52	0.39	1.07	0.98	5.78
	(-0.04, 3.09)	(-0.72, 1.50)	(0.08, 2.06)	(-0.01, 1.96)	(2.30, 9.25)
Comorbidity count	0.08	0.29	0.15	0.23	1.23
	(-0.37, 0.53)	(-0.03, 0.61)	(-0.14, 0.43)	(-0.05, 0.51)	(0.24, 2.22)
Contralateral Knee	-0.15	-0.35	-0.16	0.37	1.09
	(-1.27, 0.97)	(-1.14, 0.44)	(-0.87, 0.54)	(-0.33, 1.07)	(-1.39, 3.56)
Ankle/Feet/Toes	1.45	0.85	0.04	-0.03	0.57
	(0.20, 2.69)	(-0.02, 1.73)	(-0.75, 0.82)	(-0.80, 0.75)	(-2.17, 3.31)
Hips	0.39	-0.27	0.21	0.07	-0.02
	(-0.93, 1.70)	(-1.20, 0.66)	(-0.62, 1.04)	(-0.75, 0.89)	(-2.92, 2.89)
Elbow/Wrists/Hands	0.83	0.43	0.03	-0.21	-0.55
	(-0.37, 2.04)	(-0.42, 1.27)	(-0.73, 0.78)	(-0.95, 0.54)	(-3.19, 2.10)
Neck	1.90	1.06	0.60	0.04	1.10
	(0.42, 3.39)	(0.01, 2.11)	(-0.34, 1.54)	(-0.88, 0.96)	(-2.18, 4.38)
Shoulder	-0.42	-0.36	0.09	1.00	2.63
	(-1.79, 0.95)	(-1.33, 0.61)	(-0.78, 0.96)	(0.14, 1.85)	(-0.39, 5.66)
Spine/lower back	1.71	0.97	0.71	0.47	2.25
	(0.33, 3.09)	(0.01, 1.94)	(-0.15, 1.58)	(-0.38, 1.33)	(-0.76, 5.26)
Explained variance					
(R ² (%))	20.1	16.5	14.0	20.3	19.2

*Higher outcome score indicates worse status.

Table 4. Linear regression results; outcome: post-surgery patient-reported outcome score (statistically significant effects are bolded)*

Predictors	Model Outcome				
	Fatigue	Anxiety	Depression	Pain	Phys. Func.
Beta (Confidence Interval)					
Age	0.00 (-0.05, 0.06)	0.00 (-0.04, 0.04)	0.01 (-0.02, 0.04)	0.02 (-0.02, 0.06)	0.11 (-0.00, 0.23)
Gender (ref: female)	0.38 (-0.66, 1.42)	0.56 (-0.17, 1.29)	0.49 (-0.16, 1.14)	0.32 (-0.41, 1.05)	1.13 (-1.22, 3.48)
Education (ref:>high school)	0.37 (-0.72, 1.45)	0.38 (-0.39, 1.15)	0.27 (-0.40, 0.94)	0.18 (-0.57, 0.93)	0.60 (-1.84, 3.05)
BMI (ref: normal)					
Overweight	-1.17 (-2.55, 0.22)	-1.26 (-2.23, -0.28)	-0.49 (-1.36, 0.37)	-0.77 (-1.74, 0.20)	-1.75 (-4.85, 1.35)
Obese	-0.67 (-2.05, 0.70)	-0.90 (-1.86, 0.06)	-0.40 (-1.26, 0.46)	-0.73 (-1.69, 0.24)	-1.43 (-4.55, 1.68)
Comorbidity count	0.27 (-0.13, 0.67)	0.16 (-0.12, 0.45)	0.37 (0.12, 0.62)	0.07 (-0.21, 0.35)	0.29 (-0.62, 1.19)
Contralateral Knee	-0.07 (-1.05, 0.92)	0.20 (-0.49, 0.89)	0.16 (-0.46, 0.77)	-0.09 (-0.77, 0.59)	-0.66 (-2.86, 1.55)
Ankle/Feet/Toes	0.12 (-0.98, 1.23)	0.21 (-0.56, 0.98)	0.73 (0.04, 1.41)	1.24 (0.48, 2.00)	3.14 (0.69, 5.59)
Hips	0.04 (-1.14, 1.21)	0.00 (-0.82, 0.83)	-0.10 (-0.83, 0.64)	0.33 (-0.48, 1.15)	-0.50 (-3.12, 2.12)
Elbow/Wrists/Hands	0.20 (-0.85, 1.26)	-0.03 (-0.76, 0.70)	-0.13 (-0.78, 0.52)	-0.35 (-1.08, 0.37)	-0.41 (-2.75, 1.94)
Neck	1.37 (0.04, 2.69)	0.87 (-0.06, 1.80)	1.15 (0.33, 1.97)	1.07 (0.17, 1.98)	3.46 (0.54, 6.38)
Shoulder	0.36 (-0.84, 1.57)	0.28 (-0.57, 1.13)	0.21 (-0.55, 0.96)	-0.69 (-1.54, 0.15)	-0.28 (-2.97, 2.41)
Spine/lower back	1.23 (0.001, 2.46)	0.18 (-0.67, 1.04)	-0.03 (-0.79, 0.73)	0.46 (-0.38, 1.31)	1.83 (-0.86, 4.53)
Pre-surgery score	0.34 (0.24, 0.43)	0.61 (0.52, 0.70)	0.50 (0.41, 0.60)	0.34 (0.24, 0.45)	0.41 (0.31, 0.50)
Explained variance (R ² (%))	27.4	44.5	36.6	20.0	29.0

*Higher outcome score indicates worse status.

Table 5. Path analysis results (statistically significant effects are bolded).

Predictors	Model 1			Model 2		
	Estimate	L 95% CI	U 95% CI	Estimate	L 95% CI	U 95% CI
Outcome: Post-surgery Pain						
Age	0.020	-0.009	0.049	0.144	0.057	0.23
Gender (ref: female)	0.201	-0.351	0.753	0.161	-1.555	1.877
Education (ref: >high school)	-0.118	-0.691	0.455	0.242	-1.569	2.053
Overweight (ref: normal)	-0.385	-1.115	0.346	-0.17	-2.44	2.100
Obese	-0.355	-1.083	0.372	0.165	-2.108	2.438
Comorbidity count	-0.124	-0.337	0.089	-0.356	-1.024	0.312
Hips	0.408	-0.202	1.017	-0.761	-2.661	1.14
Neck	0.404	-0.293	1.101	0.676	-1.505	2.856
Shoulder	-0.713	-1.351	-0.075	-0.354	-2.325	1.618
Contralateral Knee	-0.162	-0.676	0.352	-0.962	-2.574	0.651
Ankle/Feet/Toes	0.972	0.390	1.554	2.29	0.466	4.113
Elbow/Wrists/Hands	-0.514	-1.068	0.039	-0.875	-2.612	0.862
Spine/lower back	0.208	-0.435	0.852	1.32	-0.684	3.324
Pre-surgery scores						
Pain; Physical function	0.251	0.166	0.336	0.253	0.173	0.334
Anxiety	0.022	-0.069	0.113	-0.066	-0.352	0.219
Depression	-0.160	-0.266	-0.054	-0.256	-0.591	0.079
Fatigue	-0.001	-0.066	0.064	0.014	-0.194	0.222
Post-surgery scores						
Anxiety	0.103	-0.006	0.212	0.282	-0.059	0.624
Depression	0.335	0.206	0.464	1.38	0.978	1.783
Fatigue	0.122	0.044	0.200	0.37	0.125	0.615
Dependant mediator variable: Anxiety						
Hips	0.052	-0.69	0.795	0.052	-0.688	0.791
Neck	0.899	0.071	1.728	0.867	0.039	1.694
Shoulder	0.128	-0.639	0.895	0.221	-0.538	0.979
Contralateral Knee	0.169	-0.447	0.786	0.177	-0.438	0.792
Ankle/Feet/Toes	0.295	-0.406	0.996	0.285	-0.415	0.985
Elbow/Wrists/Hands	-0.036	-0.708	0.636	-0.062	-0.733	0.608
Spine/lower back	0.196	-0.56	0.952	0.145	-0.606	0.896
Dependant mediator variable: Depression						
Hips	-0.069	-0.711	0.573	-0.071	-0.712	0.57
Neck	1.095	0.374	1.816	1.065	0.343	1.787
Shoulder	0.08	-0.586	0.746	0.164	-0.495	0.824
Contralateral Knee	0.119	-0.416	0.654	0.142	-0.394	0.678
Ankle/Feet/Toes	0.685	0.078	1.291	0.676	0.069	1.283
Elbow/Wrists/Hands	-0.138	-0.72	0.444	-0.163	-0.746	0.419
Spine/lower back	0.121	-0.541	0.782	0.055	-0.604	0.714

	Dependant mediator variable:			Dependant mediator		
	Fatigue			variable: Fatigue		
Hips	-0.021	-1.005	0.963	0.019	-0.951	0.99
Neck	1.482	0.385	2.578	1.469	0.385	2.552
Shoulder	0.103	-0.911	1.116	0.023	-0.969	1.015
Contralateral Knee	-0.044	-0.858	0.769	-0.132	-0.936	0.672
Ankle/Feet/Toes	0.269	-0.657	1.196	0.301	-0.614	1.216
Elbow/Wrists/Hands	0.236	-0.651	1.122	0.197	-0.678	1.072
Spine/lower back	1.114	0.114	2.114	1.115	0.132	2.099
<u>Explained Variance (R² (%))</u>						
Post-surgery_Pain; Phys Func	43.5			53.9		
Post-surgery_Anxiety	44.5			44.7		
Post-surgery_Depression	40.1			40.1		
Post-surgery_Fatigue	31.4			32.7		

Figure 1. Hypothesized mediated model (paths of specific study interest are bolded)*.

*All models adjusted for age, sex, level of education, overweight/obese, and comorbidity count (paths not shown).