Do women have poorer outcomes following total knee replacement?

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Objective: To investigate whether women have poorer pain and functional outcomes following total knee replacement (TKR) and to investigate factors that may contribute to this poorer outcome.

Methods: In a cohort of 494 people, outcomes were the Pain and Function/Daily Activity subscales of the Knee Injury and Osteoarthritis Outcome Score (KOOS) at 6 and 12 months post-surgery. Sequential multivariable regression analyses evaluated the following independent variables: (1) sex; (2) sex and age; (3) sex, age and pre-surgery score for respective outcome measures; and, (4) model 3 and body mass index (BMI), education, low back pain (LBP), depression, comorbidities, and symptomatic joint count.

Results: The sample included 323 women and 171 men. Women were significantly worse on several factors pre-surgery: pain: 39.0 vs 44.9, \( P = 0.002 \); function: 47.7 vs 55.0, \( P < 0.0001 \); depression 5.6 vs 4.7, \( P = 0.006 \); obesity (BMI \( \geq 30 \)): 54.2 vs 36.3%, \( P = 0.0002 \); and, symptomatic joint count: \( \geq 4 \): 61.3 vs 44.4%, \( P = 0.002 \). Women had worse outcomes for pain (72.2 vs 76.1, \( P = 0.04 \)) and function (75.2 vs 80.5, \( P = 0.007 \)) at 6 months. This effect was attenuated by adding pre-surgery pain/function. However, the magnitude of the association of pre-surgery pain/function was reduced when LBP, depression, BMI, education level, joint count and comorbidity count were added suggesting association with pre-surgery pain and function. Twelve month results were similar.

Conclusion: Women appear to have worse outcomes than men possibly due to a putative pre-operative profile across many factors. Consideration of TKR when impairments in pain and function are less severe along with interventions that address mood and comorbidity may improve outcomes for women having TKR.

Introduction

Pain, functional limitations, and impaired health-related quality of life are key concerns for individuals with advanced osteoarthritis (OA) of the knee. When conservative OA management has failed, total knee replacement (TKR) has been the treatment of choice\(^1\)–\(^3\). Despite being a common and cost-effective intervention associated with generally favorable outcomes\(^4\), a large proportion of individuals do not have expected outcomes following TKR\(^\text{5}\). In particular, there are reports of ongoing pain and functional impairments even up to 1 year post-TKR in 20–30% of people\(^6\)–\(^7\). Pre-surgery pain and functional status are known significant predictors of post-TKR outcomes\(^8\)–\(^13\). Among other factors, the presence of medical comorbidity\(^11\)–\(^14\), low back pain (LBP)\(^9\), obesity\(^15\)–\(^19\), concurrent OA-related pain in other joints\(^9\)–\(^10\), and mental health issues\(^20\)–\(^22\) also have been shown to influence post-TKR pain and functional status.

While there is fairly strong consensus about the influence of the aforementioned factors in predicting TKR pain and functional...
outcomes, there has been inconsistency in findings relating to the influence of sex. Some researchers have reported that women have poorer outcomes compared to men whereas others have shown that sex does not affect TKR outcomes.

Women generally report greater pre-surgery pain and functional impairment compared to men, and the reasons for this disparity are believed to be manifold. Compared to men, women often delay opting to undergo joint replacement, indicating worse pre-surgery status. However, authors variably evaluate if pre-surgery factors differ between men and women and if, considered, they likely than men to be referred to an orthopedic surgeon by their family physician, and if referred, are less likely than men to be offered surgery. Findings also indicate that women were given less medical information and less encouragement to participate in informed clinical decision making regarding undergoing TKR. It is possible that women, though generally benefitting from TKR, exhibit poorer pain and functional outcomes compared to men following TKR due to worse pre-surgery status. However, authors variably evaluate if pre-surgery factors differ between men and women and if, considered, they generally have considered only pre-surgery pain and function.

The objective of this study was to investigate whether women have poorer pain and functional outcomes at 6 and 12 months following TKR and to investigate factors that may contribute to this poorer outcome.

Methods

This study is a secondary analysis of data collected from a prospective cohort of individuals undergoing primary TKR for OA that has been previously described. In brief, individuals were recruited from four tertiary care centers in Toronto, Canada between 2005 and 2008 and followed from just prior to surgery to 1 year post-surgery. This study includes the sample of people who underwent TKR (n = 494) focusing on pre-surgery factors and the 6 and 12 month post-surgery time points. Ethics approval was obtained from each of the participating centers. Participants completed a health survey at each time point.

Outcomes: knee pain and function

The pain and function/daily living scales of the Knee Injury and Osteoarthritis Outcome Score (KOOS) were used to assess pain and function. The pain scale includes nine items assessing the frequency and the intensity of pain while performing various activities. The function/daily living scale, comprised of 17 items, asks the respondent to rate the level of difficulty experienced while performing activities of daily living. Responses on the scales are summed and normalized over 0–100 scale, with lower scores indicating worse status. The scales were administered at each time point.

Demographic and health characteristics

The survey elicited demographic information including age, sex, and level of education (dichotomized as college/university education vs high school or lower), as well as pre-surgery health characteristics. These included height and weight, from which body mass index (BMI) was calculated and operationalized as obese (BMI ≥ 30) vs non-obese (BMI < 30), symptomatic joint count (concurrent pain and/or swelling in joints other than the operated knee as indicated on a homunculus, and summed; operationalized ≥4 joints or <4 joints), comorbidity count (number of concurrent medical conditions based on no/yes responses to the American Academy of Orthopedic Surgeon’s Comorbidity scale and the absence/presence of LBP. Symptoms of depression were captured with the reliable and valid Hospital Anxiety and Depression Scale (HADS). The Depression scale includes seven items each rated on a 0–3 scale, with summed scores ranging from 0 to 21; higher scores are indicative of worse depressive symptoms.

Data analyses

Continuous data were tested confirming a Gaussian distribution. Descriptive statistics, including means and standard deviations or frequency, as appropriate, and test of differences (t-tests or chi-square), were then calculated for demographic, health variables, and for the pain and function outcome measures by sex.

Two sets of a sequential series of regression analyses were conducted with pain and function scores as the respective outcomes, with the following model covariates: (1) sex; (2) sex and age

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n = 171; 34.6%) Mean ± SD OR Frequency (%)</th>
<th>Women (n = 323; 65.4%) Mean ± SD OR Frequency (%)</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.7 ± 9.9</td>
<td>65.6 ± 10.3</td>
<td>0.05</td>
</tr>
<tr>
<td>LBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>47 (27.5%)</td>
<td>48 (14.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>124 (72.5%)</td>
<td>275 (85.1%)</td>
<td></td>
</tr>
<tr>
<td>HADS – Depression Subscale</td>
<td>4.7 ± 3.2</td>
<td>5.6 ± 4.6</td>
<td>0.006</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>109 (63.7%)</td>
<td>148 (45.8%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>≥30</td>
<td>62 (36.3%)</td>
<td>175 (54.2%)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College/University</td>
<td>115 (67.2%)</td>
<td>212 (65.6%)</td>
<td>0.765</td>
</tr>
<tr>
<td>High school or lower</td>
<td>56 (32.8%)</td>
<td>111 (34.4%)</td>
<td></td>
</tr>
<tr>
<td>Joint count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥4 joints</td>
<td>76 (44.4%)</td>
<td>198 (61.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>&lt;4 joints</td>
<td>95 (55.6%)</td>
<td>125 (38.7%)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidity count (mean, sd)</td>
<td>2.0 (1.1)</td>
<td>2.3 (1.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Pre-operative pain</td>
<td>44.9 ± 16.4</td>
<td>39.0 ± 16.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Pre-operative function</td>
<td>55.0 ± 17.5</td>
<td>47.7 ± 18.6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Notes: where numbers do not equal total n, there are missing data; Cardiovascular-related comorbidities include congestive heart failure, myocardial infarction and stroke. Abbreviations: SD – standard deviation; HADS – Hospital Anxiety and Depression Scale, depression subscale. P-values in bold indicate significant difference at P < 0.05.
### Table II

Factors associated with 6 month pain score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unstandardized beta coefficient</td>
<td>95% CI</td>
<td>P-value</td>
<td>Unstandardized beta coefficient</td>
</tr>
<tr>
<td>Sex</td>
<td>3.94</td>
<td>-4.20, 2.83</td>
<td>0.07</td>
<td>4.07</td>
</tr>
<tr>
<td></td>
<td>Female vs male</td>
<td></td>
<td></td>
<td>Female vs male</td>
</tr>
<tr>
<td>Age</td>
<td>0.12</td>
<td>-0.35, 0.59</td>
<td>0.40</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>&gt;65 years vs ≤ 65</td>
<td></td>
<td></td>
<td>&gt;65 years vs ≤ 65</td>
</tr>
<tr>
<td>Pre-surgery pain</td>
<td>0.15</td>
<td>-0.27, 0.57</td>
<td>0.47</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>&gt;30 vs ≤ 30</td>
<td></td>
<td></td>
<td>&gt;30 vs ≤ 30</td>
</tr>
<tr>
<td>LBP</td>
<td>0.32</td>
<td>0.28, 0.71</td>
<td>0.0001</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>No LBP vs LBP</td>
<td></td>
<td></td>
<td>No LBP vs LBP</td>
</tr>
<tr>
<td>BMI</td>
<td>0.13</td>
<td>-0.39, 0.64</td>
<td>0.58</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>&lt;21 vs ≥ 21</td>
<td></td>
<td></td>
<td>&lt;21 vs ≥ 21</td>
</tr>
<tr>
<td>Education level</td>
<td>0.44</td>
<td>0.27, 0.70</td>
<td>0.0003</td>
<td>0.44</td>
</tr>
<tr>
<td></td>
<td>Higher vs lower</td>
<td></td>
<td></td>
<td>Higher vs lower</td>
</tr>
<tr>
<td>Comorbidity count</td>
<td>0.40</td>
<td>0.21, 0.80</td>
<td>0.0001</td>
<td>0.40</td>
</tr>
</tbody>
</table>

CI = confidence interval; depression was measured with the subscale of the Hospital Anxiety and Depression Scale (HADS). *P*-values in bold indicate significant difference at *P* < 0.05.

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**Results**

Table I presents the description of the study participants. Of the 494 participants, 323 were women and 171 were men. A greater proportion of women were obese (54% vs 36% in men) and reported higher symptomatic joint count (61% vs 44%). Of note, more women than men also reported LBP, reported more comorbidity, and had significantly higher depression scores pre-surgery. Overall, women had greater pain and functional impairment pre-surgery (pain: 39.0 vs 44.9; function: 47.7 vs 55.0).

The cohort overall had the expected improvements of people having TKR. Women had statistically significant worse scores post-surgery at 6 (pain: 72.2 vs 76.1; function: 75.2 vs 80.5) and 12 months (pain: 76.8 vs 80.0; function 78.2 vs 82.0) compared to men, with the exception of pain at 12 months where a statistical difference was not observed.

Table II presents the results from the regression models assessing 6 month post-TKR pain scores. While sex initially was independently associated with post-surgery scores (model 1 and 2), the effect was statistically negated with the addition of pre-surgery pain to the model (model 3). In the final model, pre-surgery pain, presence of LBP, and worse depression scores were significantly associated with worse pain scores at 6 months (*P* < 0.05) (model 4). Of note the beta coefficient for pre-surgery pain reduced from 0.38 to 0.32 (16%) when these additional factors were added in model four. While sex was not significantly associated with pain scores at 12 months (Table III), older age, worse pre-surgery pain, presence of LBP, worse depression scores, and presence of comorbidities all significantly negatively impacted pain scores at 12 months post-TKR (model 4). As at 6 months follow-up, there was a decrease in the beta coefficient for pre-surgery pain (0.41–0.35 or 17%).

Table IV presents the results from the regression analyses examining function scores at 6 months post-TKR. While women had worse function scores at 6 months, the effect was no longer significant (*P* = 0.44) when pre-surgery functional status was included in the model (model 3). In the final model (model 4), older age, worse pre-surgery functional status, presence of LBP, worse depression scores, and presence of comorbidities all significantly associated with worse functional outcome at 6 months following TKR. Results at 12 months were consistent with those at 6 months (Table V). For both the 6 and 12 months results, the beta coefficient for pre-surgery function decreased from model 3 to model 4 (6 months: 0.48 to 0.35 or 27%; 12 months: 0.45 to 0.32 or 29%).

**Discussion**

The main objective of this study was to examine whether women had poorer pain and functional outcomes following TKR than men, with consideration of a number of pre-surgical factors that have been found to be associated with pain and function outcomes in the literature. We found that women had worse pain outcomes at 6 months but not at 12 months following TKR. The effect of sex on 6 months pain was attenuated once pre-surgery factors were added.
pain status was considered. Similar results were observed for function at 6 and 12 months post-surgery. This study confirms previous reports that have characterized the role of pre-surgery status in affecting outcomes of TKR\cite{13,14,22}. Our findings also are consistent with prior reports indicating that worse mental health prior to surgery is associated with poorer pain and function following TKR\cite{13,14,22,23,24}. In addition, negative influences associated with greater depressive symptoms, presence of LBP, presence of comorbidities, and more symptomatic joints which were more prevalent among women prior to surgery than men also contribute to the poorer outcomes. Overall, our findings suggest that women have a profile of putative factors prior to surgery that negatively impact their outcome, and that likely limits their potential to achieve optimal outcomes following TKR.

While some studies have suggested that women have poorer pain and functional outcomes compared to men\cite{25,26,27,28}, other literature reports no differences in post-operative outcome between men and women\cite{29,30,31,32,33,34,35}. Of the studies that found no difference in outcome by sex, three reported whether pain and function differed pre-surgery\cite{31,32,33}. All of these studies found that women had more pain and poorer function prior to surgery. However, these reports have not considered whether men and women differ pre-surgery on other factors such as obesity\cite{36,37,38}, other symptomatic joints\cite{39,40,41} and LBP\cite{42}, and psychological variables\cite{43,44,45,46}.

Of the studies that considered other pre-surgery factors that differ between men and women, as in our study, women were more obese\cite{36,37,41}. Liljensoo, however, found no difference in BMI between men and women prior to surgery\cite{47}. Similar to our work, Escobar reported that women had more symptomatic joints and LBP than men\cite{48}. We found that women also had statistically significantly worse depression scores prior to surgery compared to men as did Lingard\cite{49}. Pain can lead to greater disablement and fatigue which in turn can lead to depressive symptoms in individuals suffering from knee OA\cite{50}, which may account for the influence of psychological factors on outcome. Others, however, found no difference in psychological factors at baseline\cite{51,52}. Finally, while we found that women were on average 2 years older than men at the time of surgery, as did Liebs and Parsely\cite{31,34}, this difference is likely not clinically meaningful.

It should be noted that there are challenges in comparing our results to the literature cited above due to differences in the aspects of study outcomes and follow-up. Our data are based on patient-reported outcomes (PROs) collected at 6 and 12 months following TKR. Many of the studies in the literature used the Knee Society Rating Scale (KSS) total and or functional score\cite{53,54,55,56,57,58,59,60,61,62} or other measures\cite{63,64,65,66,67,68,69,70,71,72,73}. Others reported only PROs or a PRO in addition to the KSS\cite{69,74,75,76,77,78,79,80,81}. Additional, many of the studies included patient follow-up well beyond 1 year post TKR, up to an average of 7.3 years follow-up\cite{82}.

Table III
Factors associated with 12 month pain score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 Unstandardized beta coefficient</th>
<th>P-value</th>
<th>95% CI</th>
<th>Model 2 Unstandardized beta coefficient</th>
<th>P-value</th>
<th>95% CI</th>
<th>Model 3 Unstandardized beta coefficient</th>
<th>P-value</th>
<th>95% CI</th>
<th>Model 4 Unstandardized beta coefficient</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female vs male</td>
<td>-3.33</td>
<td>0.06</td>
<td>-6.84, 21</td>
<td>-3.25</td>
<td>0.07</td>
<td>-6.80, 29</td>
<td>-0.47</td>
<td>0.79</td>
<td>-3.85, 29</td>
<td>0.25</td>
<td>0.88</td>
<td>-3.14, 3.65</td>
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<td>&gt;65 years vs &lt;65</td>
<td>0.02</td>
<td>0.80</td>
<td>-0.10, 20</td>
<td>-0.18</td>
<td>0.04</td>
<td>-0.35, 25</td>
<td>-0.25</td>
<td>0.008</td>
<td>-0.43, 0.07</td>
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<td>Pre-surgery pain</td>
<td>0.41</td>
<td>&lt;0.0001</td>
<td>0.32, 52</td>
<td>0.35</td>
<td>&lt;0.0001</td>
<td>0.24, 47</td>
<td>0.47</td>
<td>0.008</td>
<td>1.81, 11.91</td>
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<td>LBP</td>
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<td>No vs yes</td>
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<td>Comorbidity count</td>
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</tbody>
</table>

CI = confidence interval; depression was measured with the subscale of the HADS Hospital Anxiety and Depression Scale.

P values in bold indicate significant difference at P < 0.05.
### Table IV
Factors associated with 6 month function score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unstandardized beta coefficient</td>
<td>P-value</td>
<td>95% CI</td>
<td>Unstandardized beta coefficient</td>
</tr>
<tr>
<td>Sex</td>
<td>−4.84</td>
<td><strong>0.007</strong></td>
<td>−8.34, −1.34</td>
<td>−4.83</td>
</tr>
<tr>
<td>Female vs male</td>
<td></td>
<td></td>
<td></td>
<td>−0.13</td>
</tr>
<tr>
<td>&gt;65 years vs ≤65</td>
<td></td>
<td></td>
<td></td>
<td>−0.09</td>
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<tr>
<td>Pre-surgery function</td>
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<td>0.48</td>
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<td>LBP</td>
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<td>7.63</td>
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<tr>
<td>No vs yes</td>
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<td>0.48</td>
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<td>1.08</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
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<td>−1.08</td>
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<tr>
<td>&lt;30 vs ≥30</td>
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<td>−1.08</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
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<td>−0.32</td>
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<tr>
<td>high school vs higher</td>
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<td>5.96</td>
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<tr>
<td>Joint count ≥4 vs &lt;4</td>
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<td>−0.32</td>
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<tr>
<td>Comorbidity count</td>
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<td></td>
<td></td>
<td>−0.62</td>
</tr>
</tbody>
</table>

CI = confidence interval; depression was measured with the subscale of the HADS. P values in bold indicate significant difference at *P* < 0.05.

### Table V
Factors associated with 12 month function score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unstandardized beta coefficient</td>
<td>P-value</td>
<td>95% CI</td>
<td>Unstandardized beta coefficient</td>
</tr>
<tr>
<td>Sex</td>
<td>−3.89</td>
<td><strong>0.02</strong></td>
<td>−7.29, −0.50</td>
<td>−3.83</td>
</tr>
<tr>
<td>Female vs male</td>
<td></td>
<td></td>
<td></td>
<td>−0.13</td>
</tr>
<tr>
<td>&gt;65 years vs ≤65</td>
<td></td>
<td></td>
<td></td>
<td>−0.24</td>
</tr>
<tr>
<td>Pre-surgery function</td>
<td></td>
<td></td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>LBP</td>
<td></td>
<td></td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>No vs yes</td>
<td></td>
<td></td>
<td></td>
<td>−1.08</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
<td>−1.08</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td>−0.32</td>
</tr>
<tr>
<td>&lt;30 vs ≥30</td>
<td></td>
<td></td>
<td></td>
<td>5.96</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td>−0.32</td>
</tr>
<tr>
<td>high school vs higher</td>
<td></td>
<td></td>
<td></td>
<td>5.96</td>
</tr>
<tr>
<td>Joint count ≥4 vs &lt;4</td>
<td></td>
<td></td>
<td></td>
<td>−0.32</td>
</tr>
<tr>
<td>Comorbidity count</td>
<td></td>
<td></td>
<td></td>
<td>−0.62</td>
</tr>
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</table>

CI = confidence interval; depression was measured with the subscale of the HADS. P values in bold indicate significant difference at *P* < 0.05.
not to look at differences in outcome by sex. Additionally, our sample was recruited from academic tertiary care hospitals which may limit the generalizability of the results. However, other literature indicates that there is no difference in outcome following primary TKR between tertiary and community-based institutions.

Conclusion

Our findings of significant differences between men and women on a number of pre-operative factors combined with poorer pre-operative pain and function and mental health overall suggest that women have a much more complex and putative profile prior to surgery than men. This pre-operative profile may prevent women from achieving optimal outcomes following TKR. These data would suggest that different factors need to be considered in referring women for consideration of TKR and in determining the appropriate timing for TKR surgery for men and women. Additionally, standardized acute care and rehabilitation care plans do not consider that women may have a more complex pre-operative profile compared to men, which may further limit post-surgical outcome for women.

Author contributions

Study conceptualization: Mehta, Davis, Perruccio.
Data acquisition: Davis.
Analysis: Mehta, Palaganas, Davis, Perruccio.
Manuscript writing and revision: Mehta, Palaganas, Davis, Perruccio.
Final Approval of the manuscript: Mehta, Palaganas, Davis, Perruccio.

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Competing interests
None of the authors have any competing interests in relation to this work.

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