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Comorbidities do not limit improvement in pain and physical function after total knee arthroplasty in patients with knee osteoarthritis: the BEST-Knee prospective cohort study

Lauren K King ,[1,2] Esther J Waugh ,[2,3] C Allyson Jones ,[4] Eric Bohm ,[5] Michael Dunbar ,[6] Linda Woodhouse ,[7] Thomas Noseworthy,[8] Deborah A Marshall ,[8] Gillian A Hawker ,[1,2] On behalf of the BEST-Knee Study Team

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For numbered affiliations see end of article.

Correspondence to
Dr Gillian A Hawker;
g.hawker@utoronto.ca

ABSTRACT

Objective To assess the relationship between comorbidities and amount of improvement in pain and physical function in recipients of total knee arthroplasty (TKA) for knee osteoarthritis (OA).

Design Prospective cohort study.

Setting Two provincial central intake hip and knee centres in Alberta, Canada.

Participants 1051 participants (278 in 6-minute walk test (6MWT) subset), ≥30 years of age with primary knee OA referred for consultation regarding elective primary TKA; assessed 1 month prior and 12 months after TKA.

Primary and secondary outcome measures Pre-post TKA change in knee OA pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)), physical function (Knee injury and Osteoarthritis Outcome Score (KOOS) Physical Function Short-Form) and 6MWT walking distance; and the reporting of an acceptable symptom state (Patient Acceptable Symptom State (PASS)) at 12 months after TKA.

Results Mean participant age was 67 years (SD 8.8), 59% were female and 85% reported at least one comorbidity. Individuals with a higher number of comorbidities had worse pre-TKA and post-TKA scores for pain, physical function and 6MWT distance. At 12-month follow-up, mean changes in pain, function and 6MWT distance, and proportion reporting a PASS, were similar for those with and without comorbidities. In multivariable regression analysis, adjusted for potential confounders and clustering by surgeon, no specific comorbidities nor total number of comorbidities were associated with less improvement in pain, physical function or 6MWT distance at 12 months after TKA. Patients with diabetes (OR 0.64, 95% CI 0.44 to 0.94) and a higher number of lower extremity troublesome joints (OR 0.85, 95% CI 0.76 to 0.96) had lower odds of reporting a PASS.

Conclusion For individuals with knee OA, comorbid conditions do not limit improvement in pain, physical function or walking ability after TKA, and most conditions do not impact achieving an acceptable symptom state.

Strengths and limitations of this study

- We examined the relationship between comorbidities and both the patient journey (the change from preoperative state in pain and physical function) and the destination (the postoperative reporting of an acceptable symptom state).
- We assessed a broad range of comorbidities, including several not previously examined.
- Participants were from a single Canadian province, which may limit study generalisability.
- Comorbidities were patient-reported and may be subject to misclassification.

INTRODUCTION

The number of people living with multiple chronic conditions has been rising for several decades.[1 2] This has resulted in more complex patient care decisions and a need to understand how different conditions affect one another. This is particularly important for individuals with knee osteoarthritis (OA), a common, chronic, disabling disease that frequently coexists with other common conditions such as diabetes, hypertension and heart disease.[3–5] A treatment for advanced OA, total knee arthroplasty (TKA), has become one of the most common surgical procedures in Western countries with a projected increasing trend.[6–8] Despite this, our current understanding of outcomes following TKA for individuals with OA who have comorbidities remains unclear.

The top reasons individuals with knee OA seek TKA are to improve their long-term pain and physical function.[9 10] Surgical guidelines suggest there may be less improvement in pain and physical function for individuals

with some comorbidities, including obesity, anxiety and depression.[11] A recent systematic review and meta-analysis assessing impact of comorbidities on long-term TKA outcomes found that comorbidities were associated with worse pain after TKA but had no consistent relationship with physical function. A paucity of studies and insufficient information on a number of potentially relevant conditions pointed to a knowledge gap.[12] A further limitation of prior studies is that they have largely focused on the level of joint pain or physical function achieved after TKA rather than improvement from preoperative levels. This detail is critical as the presence of comorbidities has been linked with worse levels of OA pain and function prior to TKA,[13] in other words, a lower starting point. Given the known impact of comorbidities on presurgical status, a focus on their 'journey' (improvement) may be as important as their 'destination' (final absolute level attained).[14] As the overall proportion of individuals with knee OA with comorbidities rises,[15] this knowledge is increasingly important to guide patient counselling and decision-making for individuals with complex chronic disease.

Thus, the objectives of the current study were to assess, in individuals with knee OA undergoing TKA, the relationship between specific preoperative comorbidities and number of comorbidities with (1) the change in patient-reported pain and physical function at 12 months after TKA; (2) reporting an acceptable symptom state at 12 months after TKA; and (3) the change in objectively measured walking ability at 12 months after TKA.

METHODS

Design and study sample

This was a secondary analysis of a prospective cohort study. The BEST-Knee study recruited adults age 30 years or older with primary knee OA referred for consultation regarding elective primary total knee arthroplasty (TKA) between 27 October 2014 and 30 September 2016 at two provincial central intake orthopaedic hip and knee clinics in Calgary and Edmonton, Alberta, Canada.[16 17] All surgeons (n=45) at these centres participated. Participants were required to be able to read and comprehend English. Individuals with inflammatory arthritis were excluded. The current study included those who subsequently underwent TKA and attended the 12-month follow-up visit.

Assessments

Participants completed standardised questionnaires 1 month prior to and 12 months after TKA.

Outcomes

Patient-reported knee OA pain severity was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale, where a higher score indicates worse pain.[18 19]

Knee OA-related physical function was assessed using the Knee injury and Osteoarthritis Outcome Score (KOOS) Physical Function Short-Form, coded such that a higher score indicates worse disability.[20]

Finally, participants were asked about the acceptability of their knee symptoms using the Patient Acceptable Symptom State (PASS). The PASS asks respondents to: *"Think about all the ways your knee OA has affected you during the last 48 hours. If you were to remain in the next few months as you were the last 48 hours would this be acceptable or unacceptable to you?"*

Exposures of interest

To assess comorbidities, participants indicated yes/no to the following list of conditions on the questionnaire prior to TKA: 'heart disease', 'high blood pressure', 'lung disease', 'diabetes', 'stomach disease or ulcer', 'kidney disease', 'liver disease', 'cancer', 'anemia or other blood disease', 'back pain' and any 'other medical problem'. Self-reported comorbidities have been shown to yield higher proportions of positive responses compared with medical records.[21] Those responding yes to 'other medical problem' were asked to elaborate using open-ended text. Participants were asked to indicate on a homunculus the number of lower extremity joints that had been troublesome (painful, aching, swollen or stiff) on most days of the past 3 months. Number of troublesome joints was summed (continuous variable).

The eight-item Patient Health Questionnaire Depression Scale (PHQ-8)[22] was used to assess depressive symptoms. Depressed mood was defined as a PHQ8 score ≥10/24.[22]

Reported 'other' conditions were reviewed and coded by an experienced research assistant. Other painful/disabling disorders (migraine, fibromyalgia and neurological conditions) were abstracted from open-ended responses due to potential impact on overall pain and disability.[23 24]

The total number of comorbid conditions was summed, excluding the presence of other troublesome joints in this total and categorised as 0, 1, 2 or ≥3.

Covariates

The baseline questionnaire assessed demographic characteristics including participant age, sex, level of education (post-secondary education vs no post-secondary education), current smoking status (yes/no) and level of social support (Lubben Social Network Scale[25]; higher scores indicate more support). Participants' height and weight, to calculate body mass index (BMI), were obtained from clinic records.

Assessment of walking ability: substudy

In a subset of participants, we assessed change in performance-based physical function. Walking ability was assessed using the 6-minute walk test (6MWT), a measure of submaximal functional performance, as the total distance each participant was able to walk in 6 min.

Consecutive participants at the Edmonton centre from the larger study were invited to complete a 6MWT until a target of 300 participants were recruited. 6MWT was performed within 1 month prior to TKA and 12 months after TKA. 6MWT was assessed with or without gait aids on a 20 m measured indoor loop. Rests were permitted but time was not stopped. 6MWT is part of the Osteoarthritis Research Society International (OARSI) recommended set of performed-based measures of physical function for patients with knee OA, and is considered the best available test of walking over long distances[26]; it has also shown to be reliable and responsive to interventions.[27 28]

Statistical analyses

Distributions of all continuous variables were assessed for normality. WOMAC pain scores were transformed to a score from 0 to 100. Change in pain, physical function and 6MWT (metres) were calculated by subtracting 12 month scores from pre-TKA values. Missingness of variables was assessed to confirm none > 10%[29]; imputation was not performed. Participant characteristics were summarised using frequencies, means and SD or medians and IQR, as appropriate. Characteristics of participants were compared by number of comorbidities using analysis of variance or χ^2 test, while characteristics for those who completed 6MWT versus those who did not were compared using t-tests, Wilcoxon rank-sum test and χ^2 test, as appropriate. We assessed potential multicollinearity among independent variables using variance inflation factor where values >4 indicate collinearity. None were collinear.

Our primary outcomes were change in pain and physical function at 12 months after TKA, as defined, reflecting the 'journey'. Our secondary outcome, recognising that 'destination' is also important to patients, was achieving an acceptable symptom state (PASS) at 12 months after TKA. Our exposures of interest were specific comorbidities that were hypothesised a priori to potentially limit pain or functional improvement after TKA, and included heart disease, diabetes, lung disease, depression, anaemia/haematological disorder, gastrointestinal (GI) disease, other painful/disabling disorders (as defined), back pain, cancer and total number of troublesome joints; this was based on prior evidence that a broad spectrum of conditions may impact pain and physical function both in population cohorts of older adults[30 31] and in patients with OA.[4 32] We assessed the effect of comorbidities on the primary outcomes using the multivariable generalised-estimating-equations extension of linear regression, with an exchangeable covariance matrix, to account for the potential clustering of patients within treating orthopaedic surgeons. For the secondary outcome of PASS, we used the multivariable generalised-estimating-equations extension of logistic regression. All models were adjusted for potential confounders (age, sex, BMI, education, smoking status and social support).

To assess potential compounding effects of having multiple chronic health conditions, specific comorbidities were replaced with total number of comorbidities and the models were re-run. Total number of comorbidities included those listed above, in addition to liver disease, kidney disease and hypertension and did not include total number of troublesome joints, which was included separately in the model.

An exploratory analysis was performed in the subset of patients with available 6MWT data. We assessed the impact of specific and total number of comorbidities on change in 6MWT after TKA, adjusted for confounders, using the multivariable generalised-estimating-equations extension of logistic regression as above, adjusted for potential confounders.

The quasi-likelihood under the independence model criterion (quasi-information criteria (QIC)) statistic was used for assessing model fit.[33]

All statistical analyses were performed using SAS Studio V.3.8 (SAS Institute). We presented all estimates of association with 95% CIs. Statistical significance was considered met at a two-sided p value of 0.05.

Patient and public involvement

Public involvement was first initiated during the design stage of the cohort study through interviews with patients and stakeholders. Patients and members of the public served as consultants for initial questionnaire design, methods of administration and time required for administration of the questionnaire. No patients were involved in setting the research question or the outcome measures, nor were they asked to advise on interpretation or writing up of results.

RESULTS

Participant characteristics pre-TKA

Of 1374 consenting and eligible patients who completed preoperative assessments and underwent TKA, 1276 completed the 12-month follow-up assessment. Of these, 1051 had complete data for our primary outcomes and were included in our analyses. Study flowchart is presented in figure 1. The mean age was 67 years (SD 9), 58% were female, mean BMI was 32 kg/m^2 and 57% had a post-secondary education. Prior to TKA, mean KOOS-PS was 53/100 (SD 17), mean WOMAC pain was 57/100 (SD 17), and 214/1047 (20%) participants reported an acceptable knee symptom state. Overall, 85% of participants had at least one comorbid condition. The breakdown by number of conditions was as follows: 0: 15%, 1: 28%, 2: 27%, ≥3: 29%. Prevalence of most common chronic conditions were as follows: back pain 54.4%, hypertension 53%, depressed mood 27%, heart disease 15%, diabetes 16%, lung disease 10%, cancer 6%. Participants with a higher number of comorbidities were older, had higher BMI and had worse pre-TKA scores for

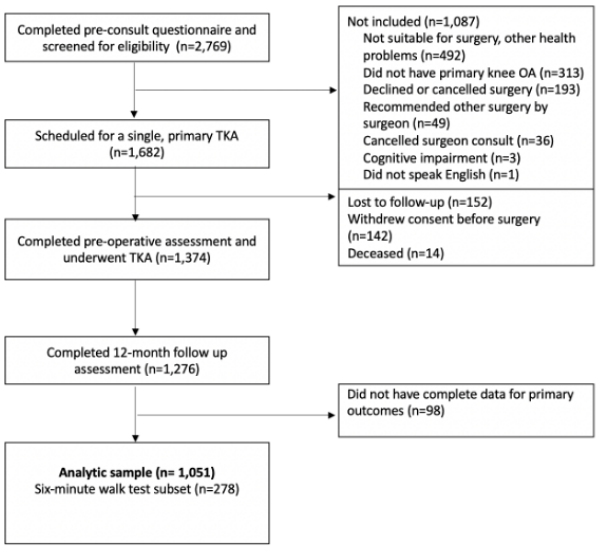

Figure 1 Study flowchart. OA, osteoarthritis; TKA, total knee arthroplasty.

pain and physical function, and shorter walking distance on 6MWT (p<0.001) (table 1).

Participant outcomes at 12 months post-TKA

At 12 months after TKA, absolute WOMAC pain score was 15 (SD 16) and KOOS score was 23 (SD 16). Participants with a higher number of comorbidities, categorised as 0, 1, 2, ≥3, had worse (higher) absolute scores for pain and physical function (p=0.02 for both) (table 1).

At 12 months after TKA, mean change in WOMAC pain was −42 (SD 17) (improvement), KOOS was −30 (SD 21) (improvement) and 913 out of 1042 (88%) reported achieving a PASS (yes) (table 1).

The amount of change in pain and physical function, and the proportion who achieved a PASS, was not different between those with 0, 1, 2 or ≥3 comorbidities (p>0.05) (table 1).

Relationship between specific comorbidities and change in WOMAC pain and KOOS physical function

In unadjusted analysis, the presence of heart disease (ß 3.42, 95% CI 0.27 to 6.56) was associated with less improvement in pain after TKA, while GI disease (ß −5.65, 95% CI −10.40 to −0.91) and depressed mood (ß −7.53, 95% CI −10.33 to −4.72) were associated with greater improvement in pain after TKA. Depressed mood (ß −10.80, 95% CI −14.04 to −7.56) was also associated with greater improvement in physical function (table 2).

Controlling for potential confounding factors, no comorbid condition was associated with reduced improvement in pain or physical function after TKA. The presence of depressed mood was associated with greater reported improvement in pain and function (WOMAC pain: ß −7.45, 95% CI −11.23 to −3.66; KOOS physical function: ß −10.80, 95% CI −14.04 to −7.56), while GI disease was associated with greater improvement in pain only (ß 5.50, 95% CI −10.08 to −0.91) (table 2).

Relationship between specific comorbidities and PASS acceptable symptom state at 12 months

In unadjusted analysis, the total number of troublesome joints (per affected joint OR 0.84, 95% 0.75 to 0.94), presence of other painful/disabling disorders (OR 0.39, 95% 0.17 to 0.92) and depressed mood (OR 0.58, 95% 0.35 to 0.95) were associated with lower odds of reporting an acceptable symptom state at 12 months.

Controlling for protentional confounders, the presence of diabetes (OR 0.64, 95% CI 0.44 to 0.94) and a greater number of lower extremity troublesome joints (per affected joint OR 0.85, 95% 0.76 to 0.96) were associated with a lower odds of reporting an acceptable symptom state at 12 months after TKA, but no association found for other specific comorbidities (table 3).

Relationship between number of comorbidities and WOMAC pain, KOOS physical function and PASS acceptable symptom state at 12 months

When specific conditions were replaced with total number of comorbid conditions, in unadjusted analysis, having ≥3 conditions was associated with greater improvement in pain. Compared with 0 condition; 1 condition ß −3.59, 95% CI −7.78 to 0.61; 2 conditions ß −4.06, 95% CI −8.67 to 0.54; and ≥3 conditions ß −4.88, 95% CI −9.47 to −0.28 (table 2). On average, there was a greater decrease (improvement) in the scores for pain in those with higher number of conditions that reached statistical significance for those with ≥3 conditions.

Controlling for potential confounding factors, results were similar. Compared with 0 condition; 1 condition ß −3.30, 95% CI −7.50 to 0.91; 2 conditions ß −3.92, 95% CI −8.84 to 0.99; and ≥3 conditions ß −5.13, 95% CI −9.89 to −0.36 (table 2).

There was no association found between number of conditions and physical function (table 2) or achievement of an acceptable symptom state (PASS) (table 3).

Results of the 6MWT substudy

A subset of 278 patients underwent 6MWT and were included in exploratory analyses. Baseline characteristics of these participants were similar to the primary cohort in all variables (online supplemental table 1). Prevalence of diabetes was lower in those who completed 6MWT (12.1%) versus those who did not (17.9%) (p=0.02); otherwise, characteristics were similar. Prior to TKA, mean 6MWT distance was 323.1 m (SD 104.7) and mean improvement in 6MWT at 12 months was 73 m (SD 91). Participants with greater number of comorbidities completed shorter 6MWT walking distance both pre-TKA and at 12 months after TKA (p<0.001 both) (table 1). However, no comorbidity was associated with having less improvement in walking distance at 12 months after TKA. In unadjusted and adjusted analyses, the presence of GI disease was associated with greater improvement in walking distance (ß 36.54 (4.82, 68.26) and ß 29.69 95% CI 0.49 to 58.88, respectively) (table 4). There was no association found

Table 1 Characteristics of participants and outcomes, overall and by comorbidity count

Characteristics	Overall (n=1051)	Number of comorbidities*				P value†
		0 (n=161)	1 (n=303)	2 (n=280)	≥3 (n=307)	
Demographics						
Mean age (years) (SD)	67.00 (8.75)/1051	64.59 (9.23)/161	66.78 (8.71)/303	66.96 (8.43)/280	68.35 (8.57)/307	<0.001
Female, n (%)	617 (58.71)/1051	90 (55.90)/161	183 (60.40)/303	163 (68.21)/280	181 (58.96)/307	0.82
Post-secondary education, n (%)	583 (56.44)/1033	94 (59.87) 157	170 (56.29)/302	153 (55.23)/277	166 (55.89)/297	0.81
Current smoking, n (%)	72 (6.94)/1038	8 (5.10)/157	22 (7.28)/302	16 (5.82)/275	26 (8.55)/304	0.45
Mean body mass index (kg/m^2) (SD)	32.43 (6.24)/1051	31.13 (5.51)/161	31.70 (6.01)/303	32.36 (6.16)/280	33.90 (6.62)/307	<0.001
Social support						
Mean Lubben Social Network Score (0–30) (SD)	17.94 (5.55)/1009	18.61 (5.66)/149	17.92 (5.43)/292	18.20 (5.18)/274	17.37 (5.90)/294	0.12
Comorbidities						
Heart disease, n (%)	144 (14.33)/1005	–	–	–	–	–
Hypertension, n (%)	522 (50.83)/1027	–	–	–	–	–
Diabetes mellitus, n (%)	162 (16.06)/1009	–	–	–	–	–
Lung disease, n (%)	99 (9.83)/1007	–	–	–	–	–
Cancer, n (%)	68 (6.97)/1002	–	–	–	–	–
Other painful disorders‡, n (%)	36 (3.43)/1051	–	–	–	–	–
Back pain, n (%)	505 (49.95)/1011	–	–	–	–	–
Depressed mood (PHQ-8 ≥10), n (%)	270 (25.84)/1045	–	–	–	–	–
Liver disease, n (%)	12 (1.21)/990	–	–	–	–	–
Kidney disease, n (%)	25 (2.50)/1001	–	–	–	–	–
Gastrointestinal disease, n (%)	113 (11.24)/1005	–	–	–	–	–
Anaemia/haematological disease, n (%)	29 (2.92)/994	–	–	–	–	–
Median total number troublesome joints (including index joint) (IQR)	2 (1, 3)/1028	–	–	–	–	–
Baseline pain and physical function						
Mean WOMAC pain (0–100) (SD)§	57.12 (17.24)/1051	50.41 (16.44)/161	56.69 (16.35)/303	58.99 (16.94)/280	59.36 (17.50)/307	<0.001

Continued

Table 1 Continued

Characteristics	Overall (n=1051)	Number of comorbidities* 0 (n=161)	1 (n=303)	2 (n=280)	≥3 (n=307)	P value†
Mean KOOS Physical Function Short-Form (0–100) (SD)§	53.08 (17.31)/1051	48.02 (17.86)/161	51.13 (14.93)/303	52.84 (16.90)/280	56.50 (17.95)/307	<0.001
12 months after TKA pain and physical function						
Mean WOMAC pain (0–100) (SD)§	15.08 (16.43)/1051	11.74 (14.89)/161	14.65 (15.86)/303	16.23 (17.25)/280	16.19 (16.80)/307	0.02
Mean KOOS Physical Function Short-Form (0–100) (SD)§	23.09 (16.12)/1051	20.08 (15.37)/161	22.39 (15.47)/303	24.36 (16.45)/280	24.22 (16.66)/307	0.02
Change from baseline at 12 months after TKA						
Mean WOMAC pain change (SD)	−42.04 (21.97)/1051	−38.67 (21.58)/161	−42.03 (22.00)/303	−42.75 (21.01)/280	−43.17 (22.90)/307	0.18
Mean KOOS Physical Function Short-Form change (SD)	−29.58 (21.33)/1051	−27.94 (21.58)/161	−28.74 (20.63)/303	−28.48 (20.25)/280	−32.28 (22.64)/307	0.07
Patient acceptable symptom state						
Baseline PASS=unacceptable (%)	214 (20.44)/1047	36 (22.36)/161	66 (21.85)/302	60 (21.66)/277	52 (16.94)/307	0.34
12 month post-TKA PASS=unacceptable (%)	919 (87.61)/1049	149 (92.55)/149	262 (86.75)/262	244 (87.46)/279	264 (85.99)/307	0.21
6MWT subsample¶						
	Overall (n=278)	**Number of comorbidities***				
		0 (n=40)	**1 (n=80)**	**2 (n=75)**	**≥3 (n=83)**	**P value**
Mean baseline 6MWT (m) (SD)	323.09 (104.66)	404.79 (83.13)	315.53 (105.76)	310.53 (98.50)	302.36 (101.45)	<0.001
Mean 12-month 6MWT (m) (SD)	395.96 (SD 111.87)	472.85 (112.07)	396.83 (106.24)	380.06 (101.51)	372.43 (111.59)	<0.001
Mean change in 6MWT (m) (SD)	72.86 (90.98)	68.07 (80.20)	81.30 (96.96)	69.52 (89.36)	70.06 (92.42)	0.81

*Sum of 12 conditions (did not include obesity or total number of troublesome joints).
†Two-tailed p value for ANOVA or χ^2 tests, as appropriate.
‡Other painful disorder defined as fibromyalgia, migraines and/or neurological disease.
§WOMAC/KOOS—higher scores indicate worse pain/function.
¶Subsample of individuals who underwent 6MWT were similar in demographic characteristics to full sample.
ANOVA, analysis of variance; KOOS, Knee Osteoarthritis Outcome Score Physical Function Short-Form; 6MWT, 6-minute walk test; PASS, Patient Acceptable Symptom State; QIC, quasi-information criteria; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Table 2 Association between specific and total number of comorbidities with change in pain, physical function and walking ability 12 months after total knee arthroplasty

	Dependent variable			
	Pre-Post change in WOMAC pain		Pre-Post change in KOOS physical function	
Independent variable	Unadjusted beta coefficient (95% CI)	Adjusted beta coefficient (95% CI)*	Unadjusted beta coefficient (95% CI)	Adjusted beta coefficient (95% CI)*
Primary model: Specific comorbid conditions				
Heart disease	**3.42 (0.27 to 6.56)**	2.59 (–1.88 to 7.07)	0.66 (–2.45 to 3.76)	0.71 (–3.67 to 5.08)
Lung disease	–1.99 (–6.76 to 2.79)	–0.90 (–5.84 to 4.03)	–1.48 (–5.99 to 3.03)	0.14 (–4.79 to 5.07)
Diabetes	–0.15 (–3.64 to 3.34)	0.62 (–2.93 to 4.18)	–0.67 (–4.90 to 3.56)	0.94 (–3.21 to 5.08)
Cancer	4.89 (–2.27 to 12.04)	3.52 (–3.70 to 10.73)	2.63 (–4.70 to 9.94)	2.29 (–4.73 to 9.32)
Back pain	–0.089 (–2.95 to 2.77)	0.57 (–2.69 to 3.83)	0.41 (–2.28 to 3.10)	0.92 (–1.84 to 3.68)
Gastrointestinal disease	**–5.65 (–10.40 to 0.91)**	**–5.50 (–10.08 to –0.91)**	–3.22 (–7.42 to 0.98)	–3.55 (–7.59 to 0.49)
Anaemia/ haematological disease	1.76 (–3.35 to 6.88)	2.13 (–4.01 to 8.27)	0.72 (–5.53 to 6.97)	1.90 (–5.95 to 9.74)
Other painful/ disabling disorders†	1.71 (–7.69 to 11.11)	1.02 (–7.49 to 9.53)	–0.31 (–8.80 to 8.17)	–1.52 (–9.57 to 6.53)
Total number troublesome joints, per joint	–0.22 (–1.12 to 0.67)	0.41 (–0.57 to 1.40)	–0.02 (–0.88 to 0.85)	0.67 (–0.36 to 1.70)
Depressed mood‡	**–7.53 (–10.33 to 4.72)**	**–7.45 (–11.23–3.66)**	**–10.83 (–14.09 to 7.57)**	**–10.80 (–14.04 to 7.56)**
		n=902 QIC 919.27		n=902 QIC 919.57
Secondary model: Number of comorbid conditions (ref=0)§				
1	–3.59 (–7.78 to 0.61)	–3.30 (–7.50 to 0.91)	–0.85 (–4.85 to 3.15)	–0.16 (–4.29 to 3.98)
2	–4.06 (–8.67 to 0.54)	–3.92 (–8.84 to 0.99)	–0.52 (–5.57 to 4.52)	–0.13 (–5.35 to 5.09)
≥3	**–4.88 (–9.47 to 0.28)**	**–5.13 (–9.89 to–0.36)**	–4.43 (–9.07 to 0.22)	–4.23 (–9.21 to 0.74)
		n=992 QIC 1000.80		n=992 QIC 1001.69

*Models adjusted for age, sex, education, smoking status and social support, as well as clustering by surgeon.
†Other painful disorder defined as fibromyalgia, migraines and/or neurological disease.
‡Depressed mood defined as PHQ-8 score ≥10.
§Total number of conditions include 12 conditions assessed (did not include obesity or total number of troublesome joints, but included kidney disease, liver disease and hypertension that were not included as specific conditions); obesity and troublesome joints included separately in model.
KOOS, Knee Osteoarthritis Outcome Score Physical Function Short-Form; 6MWT, 6-minute walk test; PHQ-8, Patient Health Questionnaire Depression Scale; QIC, quasi-information criteria; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

between total number of conditions and amount of improvement in walking distance (table 4).

DISCUSSION

In this cohort study of patients who underwent TKA for primary knee OA, we examined the relationship between comorbidities and amount of improvement in pain, function and walking ability, as well as achievement of an acceptable knee symptom state, at 12 months after surgery. Consistent with prior studies, we found that individuals with a greater number of comorbidities had worse pre-TKA and post-TKA pain and physical function.[3–5 34] However, the magnitude of their improvement in pain, function and 6MWT distance was not limited by their pre-TKA comorbidity. We also observed little impact of comorbidity on their likelihood of achieving an acceptable symptom state after TKA. These results are important for people with knee OA and their healthcare providers in decision-making regarding TKA in individuals with comorbidities.

This study importantly assesses the impact of comorbidities in patients with knee OA undergoing TKA on long-term outcomes from two perspectives: both the change from the preoperative state (the journey), as well as the

Table 3 Association between specific and total number of comorbidities with achieving a Patient Acceptable Symptom State (PASS) 12 months after total knee arthroplasty

	Dependent variable	
	Patient Acceptable Symptom State 'acceptable' 12 months post-TKA	
Independent variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Primary model: Specific comorbid conditions		
Heart disease	1.67 (0.78 to 3.49)	1.27 (0.54 to 3.02)
Lung disease	0.72 (0.23 to 1.35)	0.78 (0.34 to 1.82)
Diabetes	0.71 (0.50 to 1.01)	**0.64 (0.44 to 0.94)**
Cancer	1.46 (0.68 to 3.17)	1.04 (0.38 to 2.88)
Back pain	0.82 (0.54 to 1.23)	1.00 (0.63 to 1.59)
Gastrointestinal disease	1.56 (0.77 to 3.18)	2.19 (0.89 to 5.39)
Anaemia/ haematological disease	1.27 (0.35 to 4.70)	1.26 (0.36 to 4.35)
Other painful/ disabling disorders†	**0.39 (0.17 to 0.92)**	0.65 (0.23 to 1.84)
Total number troublesome joints to per joint	**0.84 (0.75 to 0.94)**	**0.85 (0.76 to 0.96)**
Depressed mood‡	**0.58 (0.35 to 0.95)**	0.70 (0.41 to 1.19)
		n=901 QIC 667.09
Secondary model: Number of comorbid conditions (ref=0)§		
1	0.54 (0.25 to 1.15)	0.52 (0.24 to 1.13)
2	0.57 (0.28 to 1.15)	0.57 (0.28 to 1.16)
≥3	0.51 (0.24 to 1.08)	0.53 (0.24 to 1.18)
		n=985 QIC 723.03

*Models adjusted for age, sex, education, smoking status and social support, as well as clustering by surgeon.
†Other painful disorder defined as fibromyalgia, migraines and/ or neurological disease.
‡Depressed mood defined as PHQ-8 score ≥10.
§Total number of conditions include 12 conditions assessed (did not include obesity or total number of troublesome joints, but included kidney disease, liver disease and hypertension that were not included as specific conditions); obesity and troublesome joints included separately in model.
PHQ, Patient Health Questionnaire Depression Scale; QIC, quasi-information criteria; TKA, total knee arthroplasty.

ultimate status achieved (the destination), overcoming limitations of prior research. Much focus of prior research has been on the impact of comorbidity on the absolute level of pain or physical function achieved after TKA, where patients with comorbidities have been shown to achieve lower levels of pain and physical function.[12 35–39] As previously shown by Fortin *et al*, in a cohort of patients with OA undergoing TKA, those with worse preoperative pain and function do not improve postoperatively to the level achieved by those with less pain or disability at baseline.[40] The current study clarifies that while individuals with comorbidities may begin with greater levels of pain and physical function, their capacity for improvement is not limited by their comorbidities. This is consistent with prior small studies in individuals with diabetes and depression that have assessed change from baseline,[41–43] as well as a cohort study of individuals undergoing total hip arthroplasty.[44]

Final symptom status is also important to patients.[45] Of the 10 comorbidities assessed, we found that the presence of diabetes and higher number of lower extremity troublesome joints were associated with lower odds (36% and 15%, respectively) of reporting an acceptable symptom state at 12 months after TKA. Diabetes, which has a substantial impact on physical function and health status in older adults,[46 47] has been previously shown to be independently associated with worse absolute level pain and function at 12 months after TKA compared with those without.[35–38] We did not have data on duration of diabetes or diabetes complications to better understand the contribution of these factors. Prior studies have shown that presence of other musculoskeletal comorbidities is associated with being less likely to achieve a good outcome, defined multiple ways, after TKA.[48 49]

We did not find a relationship between number of comorbid conditions and reporting less improvement in pain, function or walking distance, or being less likely to report an acceptable symptom state, after TKA. Similarly, Peter *et al*[32] did not find an association between number of conditions and pain or physical function in a cross-sectional study of patients between 7 and 22 months after TKA. In that study, however, the presence of ≥5 comorbidities was associated with a worse quality of life, measured by the physical component summary scale of the Short-Form 36. The effect of number of comorbidities on change in health-related quality of life in patients undergoing TKA was assessed by Zhang *et al*,[50] who found that patients with comorbidity (≥1 other condition) undergoing TKA experienced greater improvement in the mental component score, smaller improvements in the physical component score of the generic SF-12 measure, and similar improvements in disease-specific Oxford Knee Score, compared with those without comorbidity. They found a higher total number of comorbidities was associated with reduced gains in all measures of quality of life, although effects were small and at or below the minimally clinically important difference.[51] Other studies have found an association between greater number of comorbidities and being less likely to report a good outcome post-TKA.[48] This again suggests that comorbidities may not limit improvement, but by virtue of being associated with a worse 'starting point', they may be associated with a worse 'ending point'.

We found that for individuals with depression, improvement in pain and physical function was greater compared with those without. Since depression amplifies OA-related

Table 4 Association between specific and total number of comorbidities with change in walking ability 12 months after total knee arthroplasty

	Dependent variable	
	Pre-Post change in 6MWT distance (subsample)	
Independent variable	Unadjusted beta coefficient (95% CI)	Adjusted beta coefficient (95% CI)*
Primary model: Specific comorbid conditions		
Heart disease	1.74 (–21.51 to 24.99)	8.33 (–22.22 to 38.89)
Lung disease	13.53 (–23.28 to 50.34)	7.53 (–28.28 to 43.35)
Diabetes	–17.48 (–48.54 to 13.58)	–18.05 (–50.41 to 14.31)
Cancer	2.79 (–56.33 to 61.91)	–0.29 (–66.23 to 65.65)
Back pain	–14.78 (–37.90 to 8.34)	–19.29 (–48.83 to 10.25)
Gastrointestinal disease	**36.54 (4.82 to 68.26)**	**29.69 (0.49 to 58.88)**
Anaemia/haematological disease	–14.37 (–72.26 to 43.51)	–12.19 (–75.77 to 51.39)
Other painful/disabling disorders†	–4.69 (–58.28 to 48.91)	–10.07 (–73.02 to 52.87)
Total number troublesome joints to per joint	3.94 (–3.46 to 11.34)	5.57 (–3.57 to 14.71)
Depressed mood‡	5.54 (–16.15 to 27.23)	8.97 (–16.38 to 34.33)
		n=245 QIC 257.03
Secondary model: Number of comorbid conditions (ref=0)§		
1	13.21 (–13.13 to 39.54)	17.16 (–6.17 to 40.49)
2	0.64 (–14.99 to 16.28)	5.07 (–12.32 to 22.46)
≥3	–0.02 (–23.70 to 23.66)	2.57 (–20.81 to 25.94)
		n=264 QIC 267.32

*Models adjusted for age, sex, education, smoking status and social support, as well as clustering by surgeon
†Other painful disorder defined as fibromyalgia, migraines and/or neurological disease.
‡Depressed mood defined as PHQ-8 score ≥10.
§Total number of conditions include 12 conditions assessed (did not include obesity or total number of troublesome joints, but included kidney disease, liver disease and hypertension that were not included as specific conditions); obesity and troublesome joints included separately in model
6MWT, 6-minute walk test; PHQ-8, Patient Health Questionnaire Depression Scale; QIC, quasi-information criteria.

pain[30 52] and treating OA with TKA has been shown in prior studies to improve depressive symptoms[53] and mental well-being,[50] these patients may have experienced an additional indirect benefit to their pain experience through the lessening of their depressive symptoms. Additionally, there may be more potential for improvement when starting at a worse preoperative level. Nunez *et al* found knee OA patients with worse preoperative pain had the greatest postoperative improvement at 36-month follow-up.[54] This may also explain our finding of greater reported improvement in pain in those with ≥3 comorbidities compared with none. We also found that individuals with gastrointestinal disease had greater improvements in pain and walking distance on the 6MWT. Reasons for this are unclear. This may be due to greater engagement in physical therapy,[16] presumably due to contraindications to non-steroidal anti-inflammatories (NSAIDs), worse baseline pain due to avoidance of NSAIDs and opportunity for improvement post TKA, or due to the links between brain (depression, pain) and GI symptoms[55]-whereby GI disease is additional marker for disease severity and thus greater opportunity to improve with OA treatment. Alternatively, this may have been a spurious finding.

Strengths of this study include the breadth of chronic conditions assessed, use of established and validated outcomes for pain and physical function, and inclusion of a performed-based measure of physical function in exploratory analyses to add support to findings based on patient-reported outcomes. Characteristics, including comorbidities, of study participants are similar to other recent arthroplasty cohorts.[32] Our study has several limitations. Self-report of chronic conditions is subject to recall bias, although on average provides more comprehensive medical history than assessing comorbidities from medical records.[21] While we did not have information on severity of comorbidities, participants in the current study were already selected for and underwent TKA and thus it is unlikely they had unstable or severe symptomatic comorbidities. The sample included in 6MWT was small and therefore we may have been underpowered to detect a relationship, if present, and should be viewed as exploratory only. Finally, there are different constructs of change/difference that can be assessed.[56] In addition, while PASS can be used in different ways,[57] our study used PASS as a single item measure of patients' satisfaction with their current symptom state.

CONCLUSIONS

In our study, presence of comorbidities did not affect the amount of improvement in pain, function or 6MWT distance

at 12 months after TKA for knee OA and, except diabetes and burden of lower extremity troublesome joints, presence of comorbidities did not affect the proportion of TKA recipients who reported an acceptable symptom state. These results importantly provide more data for clinicians to draw on when discussing the appropriateness of TKA with the increasing number of patients with OA and comorbidities. Further research is needed to understand whether similar findings can be expected for patients with comorbidities being treated with non-surgical OA therapies, and the how improvement in OA pain and function may help patients with comorbidities in their chronic disease self-management.

Author affiliations
[1]Medicine, University of Toronto, Toronto, Ontario, Canada
[2]Women's College Research Institute, Women's College Hospital, Toronto, Ontario, Canada
[3]Physical Therapy, University of Toronto, Toronto, Ontario, Canada
[4]Physical Therapy, University of Alberta, Edmonton, Alberta, Canada
[5]Division of Orthopaedic Surgery and Center for Healthcare Innovation, University of Manitoba, Winnipeg, Manitoba, Canada
[6]Division of Orthopaedic Surgery, Dalhousie University, Halifax, Nova Scotia, Canada
[7]School of Physiotherapy & Exercise Science, Curtin University, Perth, Western Australia, Australia
[8]Community Health Sciences, University of Calgary, Calgary, Alberta, Canada

Twitter Gillian A Hawker @UofTDoMChair

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ORCID iDs
Lauren K King http://orcid.org/0000-0002-4721-5696
Esther J Waugh http://orcid.org/0000-0001-5499-2322
C Allyson Jones http://orcid.org/0000-0002-3952-3234
Eric Bohm http://orcid.org/0000-0002-3973-0794
Michael Dunbar http://orcid.org/0000-0003-3629-498X
Linda Woodhouse http://orcid.org/0000-0002-1615-8895
Deborah A Marshall http://orcid.org/0000-0002-8467-8008
Gillian A Hawker http://orcid.org/0000-0001-6358-1197

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